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COPYRIGHT, 1940, BY THE AMERICAN MEDICAL ASSOCIATION

ROENTGEN DOSAGE IN DERMATOLOGY EXPRESSED IN INTERNATIONAL ROENTGENS

GEORGE M MacKEE, M D

AND

ANTHONY C CIPOLLARO, M D

NEW YORK

In a previous communication before this section we¹ stated that the erythema dose for unfiltered radiation with 100 kilovolts was 300 roentgens. In the present communication we shall give the roentgen equivalents experimentally obtained for erythema doses for filtered radiations commonly used in dermatology. The majority of roentgenologists use between 550 and 700 r as the erythema dose with filtered high voltage radiations. The German roentgenologists, according to Kustner,² use 551 r plus or minus 15 per cent for the erythema dose of filtered radiations. At the Cleveland Clinic 600 r is required to produce erythema with heavily filtered roentgen rays. Pfahler³ gave 650 and 700 r for an erythema, while Failla⁴ stated that 600 r was required to produce redness with heavily filtered radiations. With 4 mm of aluminum and 127 kilovolts, Widmann⁵ used 600 r as the erythema dose. The different investigators were more in agreement in regard to the erythema dose of filtered radiation in terms of roentgens than for the erythema dose of unfiltered radiation.

Dermatologists have radiologic problems peculiar to their specialty. For the most part, even the thick and the deep lesions which the

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University.

Read before the Section on Dermatology and Syphilology at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

1 MacKee, G. M., and Cipollaro, A. C. The Roentgen Unit in Dermatology, *Arch. Dermat. & Syph.* **30**:761 (Dec.) 1934.

2 Kustner, H. Wie viel R-Einheiten entspricht die HED? *Strahlentherapie* **26**:120, 1927.

3 Pfahler, G. E., in discussion on Newell, R. R. Shall We Record and Report All X-Ray Dosages in Roentgens? *Radiology* **21**:216 (Sept.) 1933.

4 Failla, G., in discussion on Newell, R. R. Shall We Record and Report All X-Ray Dosages in Roentgens? *Radiology* **21**:216 (Sept.) 1933.

5 Widmann, B. P. Unfiltered Roentgen Rays for Cancers of Wide and Deep Involvement, *Am. J. Roentgenol.* **28**:526 (Oct.) 1932.

dermatologists treat are superficial when compared with those treated by roentgen therapists. The thickness is seldom over 4 mm. Experience has shown that for dermatologic therapy with filtered roentgen radiation 137 kilovolts and from 0.5 to 3 mm of aluminum are most desirable. There is a scarcity of material in the literature dealing with these particular factors.

THE ERYTHEMA DOSE

To ascertain the erythema dose in terms of roentgens, we selected 34 subjects at random for our studies. Fourteen of these were women and 20 were men. The ages varied from 14 to 36 years. Of these 34 subjects 21 were brunets, 9 were blonds, 2 had medium complexions, 1 had red hair and for 1 the kind of complexion was not recorded. Areas of skin 1 inch (2.5 cm) square were exposed to various intensities of radiation. Four or five areas were exposed on each person. These were on the flexor surface of the forearm or on the inner surface of the thigh. From 270 to 720 r (measured in air) was administered to each area. The kilovoltage was 137, the milliamperage 5 and the skin-focal distance 10 inches (25 cm). The filters used were 0.5, 1 and 3 mm of aluminum. A mechanical rectifying machine and a broad focus Collidge tube were used in all cases. The intensity of radiation for 0.5 mm aluminum was 120 r per minute, for 1 mm it was 112.5 r per minute, and for 3 mm it was 68.75 r per minute. The ionization instrument which we used was the Victoreen r meter.

The patients were divided into three groups. In group 1 were 10 on whom tests were made with a filter of 0.5 mm aluminum, in group 2 were 10 on whom tests were made with a filter of 1 mm aluminum, and in group 3 were 14 on whom tests were made with a filter of 3 mm aluminum. In group 1 erythema was noted in the majority of subjects with 400 r. In some blonds erythema was noted with as little as 350 r, and in brunets it was difficult to determine definite erythema with even 500 r. Each test area received from 300 to 540 r. We therefore compromised on 400 r as the erythema dose for radiation filtered through 0.5 mm aluminum.

The second group was tested with 1 mm aluminum. Five areas were selected in each subject, and to each a dose of from 400 to 720 r was administered. Erythema was noted in the majority of the subjects with 450 r. In some areas, faint redness was discerned with 400 r. Some areas receiving as much as 600 r showed only pigmentation. In some cases it was difficult to distinguish erythema from pigmentation. As a result of these observations we adopted 450 r arbitrarily as the erythema dose for radiation filtered through 1 mm aluminum.

We tested four or five areas on each subject in group 3 with doses varying from 270 to 648 r. No reaction (neither pigmentation nor

erythema) was noted in areas exposed to less than 300 r. Pigmentation preceded erythema in practically all cases. Pigmentation was noted in four to seven days and erythema was observed in from ten to fourteen days. In the majority of the tested subjects erythema was observed with 500 to 600 r. Among these it was particularly difficult to distinguish erythema from pigmentation. As a result of these observations we adopted 550 r arbitrarily as the erythema dose for radiation filtered through 3 mm aluminum.

The cutaneous changes noted in the group tested with filtered radiation were different from those noted in the group tested with unfiltered radiation. When we carried out our studies with unfiltered roentgen rays, the erythema provoked by the radiation was easily recognized. With filtered radiation some difficulties were encountered. The ery-

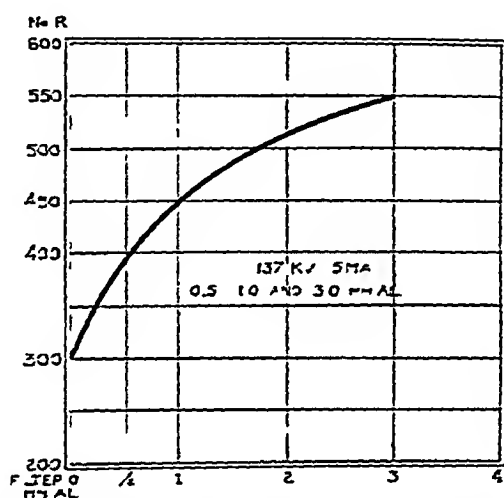


Fig 1—Curve to illustrate the relation of roentgens and erythema doses for roentgen ray qualities used in dermatology

Relation Between Roentgens and Erythema Doses for Roentgen Ray Qualities Ordinarily Used in Dermatology

| Kilovolts | Filter, Millimeters of Aluminum | Number Roentgens for Erythema | Intensity, Roentgens per Minute | Half Value Layer in Millimeters of Aluminum | Effective Wavelength |
|------------|---------------------------------|-------------------------------|---------------------------------|---|----------------------|
| 10 (Grenz) | 0 | 200 to 300 | 150 | 0.02 | 1.75 |
| 60 | 0 | 300 | 100 | 0.8 | 0.27 |
| 80 | 0 | 300 | 100 | 1.0 | 0.264 |
| 90 | 0 | 300 | 100 | 1.1 | 0.260 |
| 100 | 0 | 300 | 100 | 1.3 | 0.253 |
| 115 | 0 | 300 | 100 | 1.9 | 0.240 |
| 137 | 0.5 | 400 | 120 | 2.7 | 0.235 |
| 157 | 1.0 | 450 | 112.5 | 3.0 | 0.224 |
| 137 | 3.0 | 550 | 65.75 | 4.2 | 0.213 |

thema was not easily observed. At first the skin would show a peculiar brownish color with a tinge of redness. When the dose was increased this redness was more pronounced. With filtered radiation there was a

delay in the appearance of the erythema. It appeared in ten to fourteen days after treatment. As the thickness of the filter was increased, it was necessary to administer more roentgens to obtain erythema. The relation of the number of roentgens delivered per unit of time remained unchanged. No visible difference could be seen in the erythema produced by a "threshold dose" and that produced by a larger dose. The same difference was noted when the dose administered produced only pigmentation and was too small to cause erythema. In blonds the erythema was detected more easily than in brunets. In persons with dark complexions roentgen rays provoked a more decided pigmentary reaction. The cutaneous effects following exposure to filtered roentgen rays persisted from six weeks to several months. In all cases the reaction gradually subsided. Observation of some of these subjects several years later did not reveal radiation sequelae in the tested areas.

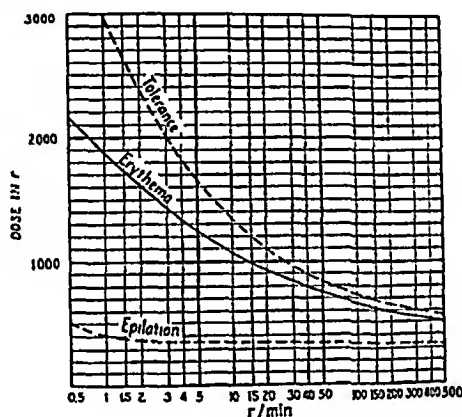


Fig 2—Relation of rate of administration of radiation to epilation, erythema and tolerance doses (Holthusen, H, and Braun, R. *Grundlagen und Praxis der Röntgenstrahlendosierung. Dosismessung und Dosisfestsetzung*, Leipzig, Georg Thieme, 1933)

The half value layer in millimeters of aluminum for 137 kilovolts and 0.5 mm aluminum was 2.7, for 1 mm aluminum it was 3.0, and for 3 mm aluminum it was 4.2. It is generally accepted that the erythema dose varies with the quality of the radiation used. Our experimental results conform with those quoted at the beginning of this paper even though the voltages we used did not exceed 137 kilovolts.

The erythema dose varies with the quality of the radiation and with the filtration. It also varies with the rate of administration of the dose. Holthusen and Braun⁶ have illustrated the time-intensity factors of roentgen irradiation in a chart (fig 2). For a given quality of radia-

⁶ Holthusen, H, and Braun, R. *Grundlagen und Praxis der Röntgenstrahlendosierung*, Leipzig, Georg Thieme, 1933.

tion, they show that erythema is produced with 500 r if the total dose is delivered in one minute. If the total dose is delivered at the rate of 5 r per minute, then 1250 is required to produce erythema.

EPILATING DOSE

The epilating dose for unfiltered radiation is 300 r. For filtered radiation it is about the same. The chart by Holthusen and Braun contains a curve for the epilating dose. It is about 350 r. Epilation occurs after this amount of radiation is administered, regardless of whether it is applied slowly, at the rate of 5 r per minute, or rapidly, at the rate of 500 r per minute. It is interesting to note also that the epilating dose does not vary with either the quality of radiation (provided it is sufficiently penetrating to affect the hair papillae) or with the filtration.

ROUTINE FILTRATION

Dermatologists employ filtered radiation for the treatment of cutaneous neoplasms, keloids and other thick or deeply seated lesions. It is the belief of some roentgenologists that filtered radiation is safer because it does not produce the intense superficial reaction caused by unfiltered softer radiation. The reaction has been found to be about the same if the intensity, the total dose and the portals are the same. The danger may be greater with filtered than with unfiltered radiation because with soft roentgen rays the reaction affects chiefly the superficial tissues, while with hard radiation the deeper tissues are injured. During the past three years we have used filtered radiation in the treatment of several hundred patients with dermatoses. Our impression is that the results were no better than those obtained with unfiltered radiation. Also it is doubtful that filtered radiation is any safer than unfiltered radiation. In the final analysis, the size and depth of the lesions to be treated should decide the quality of the radiation. Most modern shock-proof apparatus will contain inherent filters equivalent to 0.5 to 1 mm aluminum.

RADIATION QUALITY

The quality of a roentgen ray beam is best measured in actual practice by means of the half value layer, which has been repeatedly advocated as a preferential quality measure.⁷ This method has become the international standard. Formerly photometric methods were used to determine the half value layer of a roentgen ray beam. Now standard

⁷ Meyer, W. H., and Glasser, O. Erythema Doses in Absolute Units, *Radiology* 6:320 (April) 1926. Meyer, W. H., and Braestrup, C. B. Quality Determination of the Roentgen Rays, *ibid* 11:72 (July) 1928. Meyer, W. H. The Co-Relation of Physical and Clinical Data in Radiation Therapy, *ibid* 32:23 (Jan) 1939.

roentgen meters are used for this purpose. Other means of measuring ray quality are by spectroscopic examination, by measurement of the spark gap and by the use of the following formula, which holds true only for a homogeneous roentgen ray beam

$$\text{Minimum wavelength (in angstrom units)} = \frac{12\,356}{\text{kilovolts}}$$

The half value layer may be defined as the thickness of any specified metal, usually copper or aluminum, which reduces the intensity of the incident beam to one half its value. The half value layer in aluminum of a specified roentgen ray beam may be obtained by measuring the amount of absorption in successive layers of the measured metal with an iontoquantimeter. These absorbed quantities are calculated in percentage, and the figures are plotted on ordinary graph paper or on logarithmic ruled paper. The percentages are plotted along the vertical and the thicknesses of the aluminum along the horizontal. The resultant curve thus obtained is called an "absorption curve." The thickness of the aluminum required to reduce the incident beam by 50 per cent is read directly from the curve.

GRENZ RAYS

At the present time instruments of sufficient accuracy to measure roentgen rays of low voltage (6 to 12 kilovolts) are not available. Therefore it is not possible to state with any degree of accuracy the number of roentgens required to produce erythema. We have personally experimented with two commercial grenz ray chambers and with three of our own make. The results have been inconstant. Since the Bureau of Standards does not calibrate grenz ray chambers, we have been handicapped in our endeavor to learn definitely the erythema dose for these supersoft roentgen rays. We therefore have to depend largely on skin effects (the erythema dose) and electric factors for measurements of doses. There are obvious limitations to this method. If we were to estimate the number of roentgens required to produce erythema with 10 kilovolts, we would say that it was no higher than 300 r. Perhaps 200 r would be nearer to the correct value. Glasser and Portmann⁸ estimated the erythema dose for grenz rays (10 kilovolts) to be 250 r. Our results confirm their observations. We can give the exact figure only after we obtain an accurate measuring instrument.

Areas treated with 300 r showed decided erythema within forty-eight hours. After about one week pigmentation ensued and after several months this disappeared. In some cases telangiectasis, depigmentation, alopecia and atrophy developed. We have never observed,

⁸ Glasser, O., and Portmann, U. V. The Physical and Clinical Foundations of Oversoft Roentgen-Ray (Grenz-Ray) Therapy, *Am J Roentgenol* **19** 442-452 (May) 1928.

even after large doses administered over ten years ago, keratoses, ulceration or roentgen ray cancer following treatment with grenz rays

For certain superficial lesions, treatment with supersoft roentgen rays is the method of choice. However, it is our opinion, based on many years of clinical observation and experimental studies, that this soft radiation is not superior to the beta rays or the soft gamma rays of radium or to the unfiltered low voltage roentgen rays in the treatment of ordinary dermatoses. Much clinical and experimental work remains to be done with radiations below 15 kilovolts

CONCLUSIONS

1 The erythema dose for filtered radiation with 137 kilovolts and with 0.5 mm aluminum is 400 r, with 1 mm aluminum it is 450 r, and with 3 mm aluminum it is 550 r

2 The epilating dose is between 300 and 350 r and is independent of quality, filtration or intensity (roentgens per minute).

3 Filtration neither improves therapeutic results nor prevents radiation sequelae

4 The half value layer is the practical and preferred method for measuring the quality of a roentgen ray beam

5 Reliable grenz ray chambers are not available

6 We estimate that the erythema dose with grenz rays is between 200 and 300 r. The therapeutic results are no better with grenz rays than with roentgen rays ordinarily used in dermatology. Radiodermatitis can be caused by grenz rays

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ABSTRACT OF DISCUSSION

DR GEORGE C. ANDREWS, New York. I was much interested in the paper of Drs. MacKee and Cipollaro, particularly in measuring the numbers of roentgens per erythema dose with filtrations of 1 mm and 2 mm of aluminum.

It is about five years since Dr. Braestrup and I presented a paper here on a similar subject. We discussed the number of roentgens per erythema dose with unfiltered radiation and with radiation filtered through 3 mm of aluminum. At that time we stated 550 r was necessary for an erythema dose with 3 mm of aluminum.

We also at that time said that 400 r was necessary for the erythema dose with unfiltered radiation. The number of roentgens for an erythema dose with unfiltered radiation is subject to a good many influences, as Dr. Cipollaro has stated. We worked with radiation from the mechanically rectified machines, and that radiation is in general a good deal harder than that obtained from the valve tube rectified machines such as Drs. MacKee and Cipollaro, I believe, used. For that reason, it takes a larger number of roentgens to produce erythema with radiation from

mechanically rectified machines than from machines with valve tube rectification. Of course, the number of roentgens for an erythema dose is influenced by many other factors, including the size of the area treated, the time element, the number of roentgens per minute and the quality of the radiation. For that reason I disagree with the statement that the figures reported in this paper are applicable to both types of machines. I don't think that they are.

Dr Belisario of Sydney, Australia, wrote me a few days ago stating that he had been in this country, in London and in various places in Europe inquiring into the number of roentgens necessary for an erythema dose. He has been interested in that subject and was trying to get some figures and write a paper about it. He wrote, after inquiring in various places, that 400 r was what he thought was an erythema dose. So there is a little inconsistency in these results of 300 r and 400 r, which may seem considerable, but really is not so much when one considers the various discrepancies, difficulties and errors in the estimation of the dose, particularly when different equipment is used.

DR HARRY R FOERSTER, Milwaukee. Those who have witnessed or participated in the evolution of roentgen ray therapy and standardization of dosage probably appreciate the value of this contribution more fully than the younger dermatologists who are inclined to accept without question the dosage standards previously established. As a group, dermatologists are inclined to leave to others outside their specialty these important technical problems. It is gratifying, therefore, to find younger men like Drs Cipollaro and Andrews carrying on the pioneer work of Drs MacKee, Pusey and others.

Though most dermatologists use unfiltered roentgen rays, it is important to understand the technical differences involved in the use of filtered radiation. I believe the understanding of this work would be clearer if the fact were recognized that all roentgen ray therapy is actually filtered radiation therapy, for the glass wall of the air-cooled vacuum Coolidge tube presents a filter equivalent to approximately 0.5 mm of aluminum. This is the filtration reported by Dr Cipollaro for the modern shock-proof tube, so that the increasing use of the latter need not alter one's conception of doses for so-called unfiltered radiation.

The difference between the erythema effect of unfiltered radiation and radiation filtered through metal is chiefly a biologic one. The soft, or long wave, radiation that predominates in unfiltered radiation is largely absorbed by the first 2 or 3 mm of skin. This acts chiefly on the capillaries of the papillae. A relatively smaller percentage of filtered radiation is absorbed in the superficial tissues, and the erythema from such radiation is in part due to effects on deeper and larger vessels. In the latter instance the erythema is less sharply defined, and larger quantities of radiation may be introduced without marked intensification of the visible erythema effect.

The authors have directed attention to the uniformly high standards and variability of the erythema dosage in filtered radiation as determined by physicists and roentgenologists. For dermatologic purposes, except when malignant growths are being treated, it seems desirable to use the minimum or threshold erythema dose discussed by the authors, remembering that it may be doubled without marked intensification in the visible erythema but with considerable reduction in the limit of safety. If, for example, one uses 300 r, as advocated, for the erythema dose and gives a series of a dozen fractional doses in the treatment of a dermatosis, there is a far greater margin of safety in the cumulative effect than if one used 400 r as the erythema standard.

The authors have demonstrated a variability of 100 to 200 r in erythema dosage in the series of 30 cases in which tests were made by them. This should be empha-

sized, for one is too apt to accept a standardized average dose as the actual erythema dose for any given case. Goldsmith recently reported a difference in the number of roentgens required to produce erythema in 2 subjects, using the same factors in each case, greater than the difference noted for either subject when erythema tests were made with 55 and 95 kilovolts and either without filtration or with a 1 mm aluminum filter. In Goldsmith's cases the tests produced a threshold erythema at an average of 300 r in one subject and of approximately 440 r in the other regardless of kilovoltage or filtration.

My co-workers and I have standardized our erythema dose at 350 r unfiltered, at 400 r for 1 mm aluminum filter and at 450 r for 3 mm aluminum filter, as compared with Dr. Cipollaro's figures of 300, 430 and 550 r, and we have obtained erythema uniformly at those figures. It appears that whatever standard is used for the erythema dose, one must not lose sight of the individual variability in the biologic reaction to roentgen rays, and I am in favor of making test doses on every one receiving serial treatments.

The authors have called attention to the uniformity of the epilation dose with different physical factors. In view of the apparent constancy of the former with moderate variations in filtration and voltage and in the rate of irradiation, would not the epilation dose be a better yardstick for measurement of doses than the erythema dose?

I have not worked with the supersoft roentgen ray, or grenz ray, but for some years after discontinuing the use of gas tubes, from which very soft radiation was obtainable, we carried out most of our vacuum tube irradiation at 30 kilovolts, believing that better results were thus obtained in dermatoses. Because of that clinical observation I believe there is a field for supersoft radiation, such as that obtained at 12 kilovolts, but it is important to heed the warning regarding the possibilities of telangiectasia and cutaneous atrophy following the use of the grenz ray.

DR C GUY LANE, Boston. I was impressed, as I heard Dr. Cipollaro speak, with the changes which have taken place in the measurement of roentgen ray doses since the days when Dr. Pusey and Dr. Caldwell started out in this country with the measurement of doses for dermatologic conditions. Many changes have taken place, and they are still going on, and we are indebted to Dr. MacKee and Dr. Cipollaro for continuing the good work with reference to dosage with different types of filtration. There is need for further work in the comparison of the erythema and the epilation measurement of the dose with the use of modern measuring apparatus, such as the ionization chamber. They have pointed out the difficulties in estimating the erythema dose, the variations of the erythema, the consistency of the dose and its measurement by epilation. I am sure that the epilation dose, clinically speaking, is more accurate and perhaps can be widely used.

I was impressed, in a series of cases at our clinic some years ago, by the 100 per cent epilations we were having with 300 and the variation which occurred when we dropped our dose to 280 r. It did not seem possible that changing the dose to that extent might make a difference, but apparently it made a definite difference, in spite of the variation of some 20 per cent in the various subjects.

In accepting a standard dose, as was pointed out by Dr. Foerster in his discussion, one has also to think of the variation in dose used in different subjects. One should not necessarily accept such a standard for each person, for there are factors in the machine which may vary, as Dr. Cipollaro has pointed out, and also factors in the individual, such as coloration, site of involvement and previous treatment, which should be taken into consideration.

I was interested also in the possible variation in the rate of administration. Some years ago a radiologist asked me whether there was any variation in the

cellular reaction if fractional treatment was given for a longer period, that is, if one-fourth skin unit was given in sixty seconds instead of ten seconds. I have a distinct impression, although I cannot prove it, that the use of a longer distance, 16 inches (40.6 cm) for example, over a longer period of time has been better in some cases than using 8 inches (20.3 cm) for a shorter time.

DR ANTHONY C. CIPOLLARO, New York. I have here a slide which shows the absorption curves with a diagrammatic drawing of the skin on ordinary graph paper. The curves represent the degree of absorption, in successive millimeters of skin, of radiations obtained with 10, 40, 60, 80 and 100 kilovolts without filtration and 137 kilovolts with a 3 mm aluminum filter. Sixty-five per cent of the grenz rays (10 kilovolts) were absorbed by 0.5 mm of skin. At this skin level only about 10 per cent of the 40 to 100 kilovolt beams were absorbed. At the 3 mm level the grenz rays were almost entirely absorbed, whereas the 40 kilovolt roentgen ray beam was 45 per cent absorbed and the 100 kilovolt roentgen ray beam was 35 per cent absorbed. The difference in absorption at the 3 mm level is so small that theoretically the same clinical results should be obtained with the 40 and 100 kilovolt radiations. These curves indicate in a rough way the quality of radiation that is best suited for a lesion situated at a particular level. They also indicate the limitations of the various qualities of radiation used in dermatologic therapy. There is only 15 per cent absorption at the 3 mm level of the filtered roentgen ray beam (140 kilovolts and 3 mm aluminum).

For unfiltered 100 kilovolt radiation, 300 r constitutes the erythema dose. This amount also causes epilation of the hair of the scalp in children. The definition of an erythema dose should contain a statement to cover epilation.

Dr. Andrews is right in saying that there is a difference in the number of roentgens required to produce erythema with different machines. Fewer roentgens will produce erythema with a valve rectified machine than with one mechanically rectified. This applies only to unfiltered radiation. With filtered radiation, there is no difference because the softer rays are absorbed by the filtering material.

I am glad that Dr. Lane called attention to the difference in epilation between 300 r and 280 r. That has been my experience. When the statement is made that radiation with 300 r is sufficient to produce erythema, the implication is that this quantity also causes epilation. With valve tube machines, erythema with an unfiltered 100 kilovolt roentgen ray beam may be obtained with as little as 226 r, and this quantity is not sufficient to cause epilation.

ELEPHANTIASIS OF THE LIPS AND OF THE MALE GENITALIA

WITH SPECIAL REFERENCE TO SYPHILIS AND LYMPHOGRANULOMA
VENEREUM AS ETIOLOGIC FACTORS

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AND

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Elephantiasis is a chronic disease of the cutaneous and subcutaneous tissues. It is characterized by inflammation and obstruction of the lymphatic vessels and subsequent hypertrophy and hyperplasia of the fibrous connective tissue. The lymph stasis and the resulting pachydermia produce persistent enlargement and gross deformity of the affected part of the body. The regions of predilection are the lower extremities and the external genitalia, the upper extremities, lips, ears and eyelids are less frequently affected. Elephantiasis may be congenital or acquired, but in this communication only certain acquired types will be considered.

Elephantiasis may be caused by many different factors. The etiologic importance of *Filaria sanguinis hominis* in endemic elephantiasis is well known. Removal of large amounts of lymph gland-bearing tissue in the surgical treatment of malignant tumor or of certain infections of the lymph nodes may be followed by chronic lymphedema and subsequent elephantiasis. Neoplastic processes of the lymph glands, Hodgkin's disease, chronic streptococcic lymphangitis, tuberculous and syphilitic adenitis and the lymphadenitis of lymphogranuloma venereum are common diseases producing lymph stasis that may terminate in elephantiasis.

In the era preceding the discovery of *Spirochaeta pallida* and the serologic reactions for syphilis and also before the advent of modern antisypilitic remedies, syphilologists considered syphilis one of the principal causes of elephantiasis of the lips and of the external genitalia. Chronic ulcers of the vulva with elephantiasis, or "esthiomene of

From the Cleveland Clinic

Read at the Sixty-Second Annual Meeting of the American Dermatological Association, Inc., Monte-Bello, Quebec, Canada, June 2, 1939

Hygumel,"¹ which is frequently accompanied by stricture of the rectum (the anorectal syphiloma of Fournier) was until a decade or so ago considered due to syphilis. Likewise, a chronic edematous condition of the lips described by Mracek and Lang² in 1888 and thirteen years later discussed in detail by Fournier³ under the title of diffuse hypertrophic syphiloma has been referred to in the literature as syphilitic elephantiasis of the lips.

Since the recognition of lymphogranuloma venereum as a distinct entity and the discovery of a specific diagnostic test for this disease by Frei,⁴ many reports have appeared which show conclusively that esthiomene and the anorectal syndrome described by Fournier are not due to syphilis but are manifestations of lymphogranuloma venereum. Also, recent reports indicate that the type of elephantiasis of the penis and scrotum that had heretofore been thought to be due to syphilis is in some cases analogous to esthiomene.

Some years ago, one of us (E. W. N.) observed 2 syphilitic patients with elephantiasis of the penis and scrotum. In neither case could the elephantiasis be explained on a basis of lymph stasis caused by any gross change in the superficial inguinal lymph glands. One patient had positive serologic reactions and neurologic signs which were consistent with the diagnosis of tabes dorsalis, the other patient had a positive Wassermann reaction of the blood and a history of an old syphilitic infection. A study of these patients was impossible, as they were observed only once. A few years later 2 other syphilitic patients were observed, each of whom presented, among other signs of the infection, an unusual persistent edematous enlargement of the lower lip. In both cases the clinical picture was identical with Fournier's description of diffuse hypertrophic syphiloma. More recently we have had the opportunity of studying a patient with elephantiasis of the penis and scrotum which was similar to that seen in the 2 cases aforementioned.

Elephantiasis of the type observed in these cases is rare. Fournier's description of syphilitic elephantiasis of the lip has apparently escaped the notice of authors of American textbooks on dermatology and syphilology for the past two or three decades, and the more recent works either contain brief comment only or fail to mention syphilis as a

1 Cole, H. N. Lymphogranuloma Inguinale, Fourth-Venereal Disease. Its Relation to Stricture of the Rectum, *J. A. M. A.* **101**:1069-1076 (Sept. 30) 1933.

2 Mracek and Lang, cited by Petrov. Sur l'éléphantiasis syphilitique, *Ann. d. mal. vén.* **10**:337-355, 1915.

3 Fournier, J. A. Traite de la syphilis. Tertiaire période, Paris, J. Rueff, 1901, pp. 250-253.

4 Frei, W. Eine neue Hautreaktion bei Lymphogranuloma inguinale, *Klin. Wchnschr.* **4**:2148-2149 (Nov. 5) 1925.

cause of elephantiasis. There are numerous reports pertaining to syphilitic elephantiasis, but with the recognition of lymphogranuloma venereum as a distinct entity and with better understanding of its various clinical manifestations the majority of these reports have become antiquated, and the importance previously attributed to syphilis as a cause of elephantiasis has greatly decreased. It now seems apparent that in some of the cases which have been reported as instances of syphilitic elephantiasis of the male genitalia the elephantiasic condition was in reality a manifestation of lymphogranuloma venereum. We have found few reports of cases in which syphilis could be considered the principal cause. Elephantiasis complicating extensive ulcerative gummatous infiltrations of the leg is most probably the result of secondary streptococcic lymphangitis.

In view of the present day concept that in some instances elephantiasis of the penis and scrotum is analogous to esthiomene, it would seem that inclusion of examples of Fournier's diffuse hypertrophic syphiloma in this discussion is unwarranted. This objection is only partially justified, because until recently both these conditions were considered by most observers to be syphilitic elephantiasis. Likewise, the pathogenesis of the type of elephantiasis of the lip under consideration is still undetermined, and there is reason to suspect that future observations may show lymphogranuloma venereum to be the chief etiologic factor in both these conditions.

The purposes of this report are (1) to report 2 cases of the rare type of hypertrophy of the lips described by Fournier, (2) to report a case of elephantiasis of the male genitalia probably caused by lymphogranuloma venereum and (3) to discuss the similarity and probable relation between these two conditions.

SYPHILITIC ELEPHANTIASIS OF THE LIP

Review of the Literature—In 1893, Eichhorst⁵ reported a case of soft elephantiasis of the lips due to syphilis. The patient was a man who had had several mucocutaneous relapses, and during the fourth year of the infection redness of the nose and edema of the upper lip developed. The swelling spread to the lower lip, which became greatly deformed and reached the thickness of 2 thumbs. There were excessive salivation and bilateral rhagades. On palpation the lower lip was found to be soft and elastic. The swelling was painless. The submaxillary lymph nodes were enlarged but not tender. There was no fever and no history of recurrent erysipelas. While under observation the scrotum became enlarged but this swelling disappeared later after the use of

⁵ Eichhorst, H. Elephantiasis syphilitica der Lippen, *Virchows Arch. f. path. Anat.* **131**:568-573, 1893.

large doses of potassium iodide. The edema of the lips improved on administration of a mercury compound but recurred after the treatment was discontinued. Eichhoist stated that there were no true syphilomas of the lip in this case. He considered the swelling of the lip as soft elephantiasis due to syphilis and pointed out that syphilitic elephantiasis does not respond well to treatment.

Fournier³ observed 15 cases in each of which chronic doughy edema of the lips produced such a striking change in the appearance of the patient that he thought the disease merited special consideration. His description of this deformity is excellent and detailed. He observed the condition only in the late stage of syphilis, usually between the tenth and the sixteenth year of the infection. In 12 cases only one lip was involved, in the remaining 3 both lips were enlarged. The swelling was limited to the lower lip in 10 cases. The massive enlargement of both lips produced a bizarre deformity of the mouth which was observed best in profile view, the lower lip appearing to be rolled outward. The lips retained their general form, and the color of the skin was unchanged. In some cases the mucous membrane of the lower lip showed indentations produced by pressure against the teeth. The enlarged lips were soft, could not be pitted and on palpation felt clammy and elastic. The enlargement was accompanied by drooling and by difficulty in articulation and mastication. The regional lymph glands were not enlarged, and there was no pain, either spontaneous or provoked. The onset of the edema was insidious, but after the condition was fully established the size of the lips remained constant for years. In 1 of Fournier's patients the hypertrophy had transformed the lower lip into a sausage-like mass that had remained unchanged for eight years. Late cutaneous syphilids involving the nose and chin were coexisting lesions in some cases, and frequently there was an accompanying sclerous form of late syphilitic glossitis which the author thought was in some way related to the enlargement of the lip. He referred to a case that Miacek had observed in which the lesion invaded the nose and tongue. Fournier was unable to obtain a complete cure of the condition, but in some cases the hypertrophy was noticeably decreased on intensive treatment with potassium iodide, injections of mild mercurous chloride and continuous compression by an india rubber dressing.

Whitfield⁶ reported a case of chronic enlargement of the lips due to syphilitic lymphangitis similar to that observed by Fournier. The patient was a man who had a syphilitic infection of fourteen years' duration. During the eighth year extensive late syphilids developed on the legs, and three years later the lips and the prepuce became swollen.

6 Whitfield, A. Chronic Enlargement of the Lips Due to Syphilitic Lymphangitis, *Proc Roy Soc Med (Dermat Sect)* 2 99-102, 1908-1909.

A large part of the prepuce had been excised, but there still remained a certain amount of elephantiasis of the penis. When the patient was first seen by Whitfield there were an enormous enlargement of the lips (particularly of the lower lip), ulcers of the commissures of the lips, impetiginous syphilids in the scalp and chronic superficial syphilitic glossitis. The glossitis and cutaneous lesions responded favorably to antisymphilitic treatment. The lips became more pliable and comfortable, but the deformity did not disappear. Whitfield felt that the labial enlargement was caused by syphilitic lymphangitis. In the discussion of this case Macleod referred to 2 similar cases which he had observed and stated that it is difficult to treat such conditions successfully. The coexisting elephantiasis of the lips and of the penis in this case was probably not accidental. The significance of this observation will be discussed later.

Montgomery and Culver⁷ reported a case of hypertrophy of the lower lip associated with late nodular syphilids on the chin and at the commissures of the lips. The syphilomas disappeared rapidly after the administration of arsphenamine, but the residual elephantiasis disappeared slowly. This case differs from ours and from those reported by Fournier and by Whitfield in that the enlargement of the lip was due to gummatous infiltrations, however, the elephantiasis which remained after the rapid disappearance of the nodular syphilis probably was similar to that observed in other cases.

Under the title "Syphilome en nappe" Tuffier⁸ described and differentiated in detail a tertiary lesion of the lip characterized by uniform hypertrophy with moderate induration, superficial ulcerations of the mucosa and red-violet pigmentation of the skin. In some weeks the lip became everted and enlarged to two or three times its normal size. Untreated, the lip after months showed scarring and atrophy, with an irregular lobulated contour. In the early stages of the condition the lesion could be made to disappear by antisymphilitic treatment, but after it became sclerosed it did not respond.

Some observers have confused this lesion with the diffuse hypertrophic syphiloma of Fournier, although there is only a superficial resemblance.

New and Kirch⁹ reported 67 cases of chronic noninflammatory permanent enlargement of the lips and face which they concluded was a

7 Montgomery, D. W., and Culver, G. D. Enlargement of the Lower Lip from Syphilis, *Am J Syph* 6 55-57 (Jan) 1922

8 Tuffier. Gommès et scléroses syphilitiques des lèvres. Labialites tertiaires, *Rev de chir* 6 777-812, 1886

9 New, G. B., and Kirch, W. A. Permanent Enlargement of the Lips and Face Secondary to Recurring Swellings and Associated with Facial Paralysis. A Clinical Entity, *J A M A* 100 1230-1233 (April 22) 1933

clinical entity. The lips and cheeks were most frequently involved by a diffuse, soft nonpitting swelling. Peripheral paralysis of the facial nerve occurred in 13 cases. Histologic examination showed only edematous tissue containing lymphocytes. The cause of the edema was not determined, however, the authors stated that general examination revealed nothing that might bear any relation to the condition. They did not state the incidence of syphilis in their cases, and there is no reason to think that they considered lymphogranuloma venereum a possible etiologic factor. The edema in these cases was similar to that associated with diffuse hypertrophic syphiloma, but apparently concomitant manifestations of late syphilis were absent in all cases. Paralysis of the facial nerve is not a part of Fournier's syndrome.

Reference should be made to a case presented by Weidman and Hunter¹⁰ before the Philadelphia Dermatological Society. The patient was a Negro aged 35 years who had had edema of the eyelids for five years as well as edema of the penis and scrotum and a generalized patchy pigmentary eruption. The Fiea reaction was positive and the albumin-globulin ratio was reversed. Weidman raised the question whether the edema was one more cutaneous manifestation of lymphogranuloma venereum.

Fournier's diffuse hypertrophic syphiloma is a rare condition. We were unable to find a case of this condition reported in the American literature. The following 2 cases have been observed at the Cleveland Clinic.

REPORT OF CASES

CASE 1—A white man aged 42 was admitted to the clinic on Oct 4, 1926. His chief complaint was swelling of the lips. The family and marital histories were unimportant. In 1903, a penile lesion developed after coitus. It was cauterized and treated with topical remedies. The patient had never received antisyphilitic treatment.

In 1925, after some dental work, one side of the lower lip began to swell. The swelling gradually spread to involve the whole lip. A few days before we first saw him the upper lip began to enlarge and a fissure appeared at the left corner of the mouth. The swelling of the lips had been painless. At no time had he had erysipelas or recurrent attacks of acute cellulitis of the face or lips. Applications of heat and one roentgen ray treatment (dose unknown) had failed to alter the swelling.

The patient was well developed and well nourished. With the exception of hypertrophy of the lower lip, physical examination gave normal results. The lower lip was diffusely enlarged to approximately twice its normal size, with little change in its general outline. It was soft and elastic, it could not be pitted, and its cutaneous surface was normal in color. In profile the lower lip appeared to be rolled outward. The vermilion margin was smooth but considerably

10 Weidman, F. D., and Hunter, R. Lymphogranulomatosis Inguinalis. Edema of the Eyelids of Undetermined Nature, *Arch Dermat & Syph* 34:342 (Aug) 1936.

enlarged Because of an excessive flow of saliva there was a superficial, perlèche-like erosion at the left commissure of the lips The upper lip was slightly enlarged The submaxillary lymph glands were not enlarged, and there were no signs of gummatous infiltration of the skin of the lips or of the face The Wassermann and Kahn reactions of the blood were strongly positive (4 plus) Other laboratory tests revealed no abnormality Biopsy was not performed

A diagnosis of syphilitic elephantiasis of the lower lip was made, and anti-syphilitic therapy was started From Oct 11, 1926 to March 26, 1927 the patient received four injections of potassium bismuth tartrate (0.4 Gm), four injections of mercury salicylate (0.26 Gm) and seven injections of neoarsphenamine (5.4 Gm) Increasing doses of saturated solution of potassium iodide were taken by mouth As this amount of antisyphilitic medication produced only a slight decrease in the size of the lip, the patient became discouraged and discontinued treatment He has not been observed since

CASE 2—A white man aged 32 came to the clinic on Nov 22, 1933, complaining of an eruption on the left arm and left hand and an enlargement of the lower lip His family history and marital history were not important Gonorrhea and syphilis had been contracted in 1920 The only antisyphilitic treatment which he had received consisted of four intramuscular injections in 1920

About one year before he was first seen the lower lip was bruised in a fist fight, but the mucocutaneous surfaces were not broken The lip was painful and swollen for a week One month later the lower lip began to increase in size, and up to six months before we saw him there were periods of remission and exacerbation Since then there had been a gradual enlargement There were no subjective symptoms, and the hypertrophy of the lip was not preceded by erysipelas

A month previously he had injured the left hand, and an eruption developed at the site of the injury He had recently been treated by his family physician for "ringworm" infection on the left arm

The hypertrophy of the lip and the cutaneous lesions were the only significant abnormalities found on physical examination On the dorsal surface of the left hand and the extensor surface of the left arm were late nodular ulcerative syphilids There was a dull red, granulomatous nodule involving the skin in the middle of the upper lip A painless, soft, elastic, diffuse enlargement of the lower lip gave the patient a bizarre appearance (fig 1) No nodules or other clinical evidences of a granulomatous infiltration were found in the lower lip The lip maintained its normal form and could not be pitted or decreased in size by compression The labial eversion emphasized by Fournier was well demonstrated and was seen best in the profile view There was a smooth, irregular atrophic scar on the enlarged vermilion surface of the right side of the lower lip The submaxillary glands were not enlarged The Wassermann and Kahn reactions were strongly positive The patient refused to submit to a lumbar puncture or to permit a biopsy

A clinical diagnosis of late cutaneous syphilis and syphilitic elephantiasis was made, and antisyphilitic treatment was begun The patient discontinued treatment after he had received six intramuscular injections of bismuth salicylate Potassium iodide was taken by mouth The syphilids responded favorably to treatment, but at our last observation we were unable to detect any improvement in the hypertrophy of the lower lip The patient was advised to have the deformity of the lip surgically corrected, but he would not consent Although this patient presented unmistakable manifestations of late cutaneous syphilis, it is regrettable that a test with Frei antigen was not made

In our opinion the hypertrophy of the lip in these 2 cases was identical with Fournier's diffuse hypertrophic syphiloma. The process began in the lip and progressed rapidly until the lip was twice its normal size. The hypertrophy did not destroy the normal form of the lip and remained unchanged in spite of antisyphilitic treatment. The enlarged lip was not indurated, instead, it was soft, elastic and doughy and did not pit on pressure. The regional lymph glands were not enlarged. We were unable to find a lesion in the mouth or in the neck which would explain the elephantiasis. We believe that absence of acute febrile reactions or attacks of erysipelas preceding the hypertrophy was sufficient reason for excluding the possibility of elephantiasis nostras. The

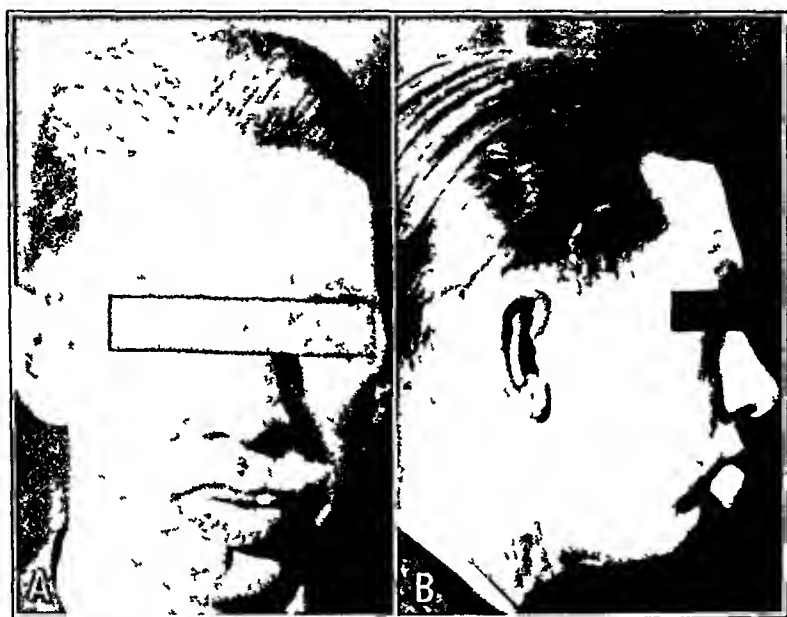


Fig 1 (case 2) — *A*, Hypertrophy of the lower lip with a small gummatous nodule on upper lip. *B*, eversion of the lower lip.

doughy, elastic feel of the lip, the rapid appearance of the hypertrophy and the fact that the lip retained its normal form made the diagnosis of lymphangioma untenable.

In our 2 cases the point of interest is the questionable importance of syphilis in the causation of elephantiasis. The inefficacy of modern antisyphilitic remedies in this condition not only suggests that the pathologic changes in the lip were not gummatous but arouses suspicion as to the importance of syphilis as an etiologic factor.

SYPHILITIC ELEPHANTIASIS OF THE MALE GENITALIA

Until a few years ago the same uncertainty existed regarding the importance of syphilis as a cause of elephantiasis of the genitalia.

Numerous cases of syphilitic elephantiasis of the penis and scrotum have been reported, but in only a few which we have reviewed was there sufficient evidence to warrant such a diagnosis

Edema of the male genitalia terminating in elephantiasis may be initiated by a syphilitic infection in one of the following ways

- 1 By extensive syphilitic adenitis of the inguinal and pelvic lymph nodes
- 2 By diffuse syphilitic inflammation of the prepuce and scrotum
- 3 By pure syphilitic lymphangitis of the genitalia
- 4 By ulcerative syphilids of the leg or of the genitocrural region complicated by secondary streptococcic lymphangitis

The first two conditions are rare, and it is doubtful whether a syphilitic inflammatory reaction limited mainly to the lymphatics ever occurs. In many of the reported cases of so-called syphilitic elephantiasis of the penis and scrotum which we have reviewed complicating streptococcic lymphangitis was the most probable cause. We have eliminated all cases reported as instances of syphilitic elephantiasis of the male genitalia in which it seemed that secondary streptococcic lymphangitis was the major etiologic factor. However, rare cases of elephantiasis of the penis and scrotum have been reported in which it was reasonably certain that syphilis was the true cause.

Review of the Literature—In a comprehensive discussion of elephantiasis, Petrov¹¹ stated that syphilis does not play as important a role in the causation of elephantiasis as has been maintained by many observers. He pointed out that syphilitic elephantiasis ordinarily develops in the tertiary stage of the disease and that the genitalia were affected in 32 per cent of cases studied by him, while the lip was involved in only 15 per cent. Petrov reported a case of syphilitic elephantiasis of the penis and scrotum. The genitalia were three times their normal size. The skin of the scrotum was bluish and indurated and did not pit on pressure. There was no pain. There were numerous verrucous elevations separated by sulci from which could be expressed a seropurulent exudate. On the clinical findings the diagnosis rested between syphilis and tuberculosis. Cultures of material obtained from the sulci showed only staphylococci. The von Pirquet reaction was negative, but the Wassermann reaction was positive. The histologic changes consisted of hypertrophy of the connective tissue, dilatation of the blood and lymphatic vessels and perivascular infiltration with small lymphocytes, mast cells and plasma cells. There were pronounced endarteritis and endophlebitis. After two months of antisypilitic

¹¹ Petrov. Sur l'éléphantiasis syphilitique, *Ann d mal vén* 10:337-355, 1915

treatment with potassium iodide and mercury compounds the penis was of normal size, but the scrotum had decreased to half its original size. The verrucous elevations were unchanged. The induration of the skin of the scrotum had not completely disappeared. The author stated that in syphilitic elephantiasis antisyphilitic therapy does not diminish the affected organs beyond a certain point.

McDonagh¹² observed a man aged 46 in whom eighteen years after syphilis was contracted, nonulcerative late syphilis developed on the buttock and on the left half of the scrotum. One year later the scrotum began to enlarge. Eleven years afterward, when this patient came under observation, the syphilids of the scrotum had disappeared, but there was superficial glossitis. The penis was buried in an enlarged scrotum which measured $28\frac{1}{2}$ inches (72.4 cm) in circumference. The Wassermann reaction was positive. After thirteen injections of gray oil (a mixture of olive oil and hydrous wool fat, containing mercury) the scrotum measured $13\frac{1}{2}$ inches (34.2 cm) in circumference, the skin was softer and the testicles and penis were normal. Histologic changes in the scrotum consisted chiefly of a decided increase in connective tissue elements, dilated lymph spaces surrounded by a layer of endothelial cells and infiltrations of lymphocytes and plasma cells. The arteries and veins were practically unchanged. McDonagh stated the opinion that this case was an example of syphilitic lymphangitis. In his discussion Pringle stated that he had been unable to find definite evidence of syphilitic lymphangitis recorded in the literature.

Emery and Glantenay¹³ reported the case of a man aged 45 with a syphilitic infection of twenty years' duration in whom severe edema of the prepuce developed suddenly and without apparent cause. After a series of partial remissions the prepuce gradually became thickened and sclerosed. At the end of two years the penis was two or three times its normal size, and the scrotum began to enlarge. Ten years prior to the onset of the edema, late nodular syphilids appeared on the thighs and buttocks and later on other parts of the body. The enlargement of the genitalia was without pain or evidence of an acute inflammatory reaction in the skin of the penis or that of the scrotum. The authors pointed out that the onset and clinical characteristics of the elephantiasic condition in this case were identical with those seen in cases of diffuse hypertrophic syphiloma of the lip. In a discussion of this case Fournier stated that he was convinced that the lesions were syphilitic and that

12 McDonagh, J. E. R. Syphilitic Elephantiasis of the Scrotum (Lymphangitis), *Brit J Dermat* 24 24-27, 1912.

13 Emery and Glantenay. Éléphantiasis des organes génitaux externes, *Bull Soc franç de dermat et syph* 9 150-151, 1898.

the syphiloma of the lip offered comparable characteristics. Although the effect of antisyphilitic treatment was not recorded, it should be pointed out that the mode of onset, the coexisting late syphilids and the character of the elephantiasis were similar to those of diffuse hypertrophic syphiloma of the lips.

Levy-Bing and Gerbay¹⁴ reported 2 cases of elephantiasis of the male genitalia which they considered to be uncontestedly of syphilitic origin. The first case was that of a man aged 26 in whom elephantiasis or edema of the scrotum developed during the secondary stage of syphilis. There were two chancres on the scrotum and one on each side of the median raphe. The scrotum was twice its normal size, and there was marked edema of the skin in the pubic region. There was a decided bilateral enlargement of the lymph glands. The extensive regional syphilitic lymphadenitis was the cause of the lymphedema of the scrotum. The authors stated that this case was an example of an uncommon yet well known type of syphilitic elephantiasis of the genitalia. In this type the elephantiasis is always secondary to a preexisting syphilitic lesion.

Their second patient was a man aged 22 in whom severe edema of the penis and scrotum developed without any preceding or concomitant lesion of the skin or mucous membrane. In each inguinal region there were four or five firm, movable lymph glands the size of small almonds. The Wassermann reaction was strongly positive. With antisyphilitic treatment there was a prompt return of the genital organs to their normal size.

These cases were reported as examples of syphilitic elephantiasis. It seems to us that changes characteristic of elephantiasis were not present and that syphilitic lymphedema would be a more accurate term.

The only acceptable case of syphilitic elephantiasis of the male genitalia which we found in the American literature was a case reported by Marshall¹⁵. The patient was a Negro aged 30 in whom an enlargement of the genitalia developed thirteen years after he had contracted syphilis. There were no concomitant late syphilids. A careful search for streptococci in the skin of the scrotum was made, but none were observed. The superficial lymph glands were enlarged. The Wassermann reaction of the blood was strongly positive. The skin of the genitalia was firm and thickened and did not pit on pressure. The histologic changes consisted mainly of increase in the fibrous connective

14 Levy-Bing and Gerbay. Deux cas d'elephantiasis syphilitique des organes genitaux, *Ann d mal ven* 13 600-609, 1918.

15 Marshall, C. H. Syphilitic Elephantiasis of the Scrotum, *J A M A* 85: 875-877 (Sept 19) 1925.

tissue and perivascular infiltration with small lymphocytes plasma cells and a few mast cells. There were numerous dilated lymph spaces, and many of the smaller arterioles were obliterated. Prompt and decided improvement followed antisymphilitic treatment.

Apparently there is little doubt that in rare cases elephantiasis of the male genitalia is of syphilitic origin. However, for years various observers have reported cases of sporadic elephantiasis of the penis and scrotum in which no definite etiologic agent could be found. In some cases there were unmistakable concomitant signs of syphilis but antisymphilitic treatment failed to influence the elephantiasis. In others there was no adequate explanation for the enlargement of the genitalia. It is probable that the elephantiasis which was erroneously considered to be of syphilitic origin in some of these cases was actually caused by the virus of lymphogranuloma venereum.

ELEPHANTIASIS OF THE MALE GENITALIA DUE TO LYMPHOGRANULOMA VENEREUM

Review of the Literature—Barthels and Biberstein¹⁶ were the first to point out that in rare cases an existing lymphogranulomatosis inguinalis may cause an elephantiasis of the male genitalia which is a counterpart to esthiomene. Their patient was a man aged 31 who at the age of 21 had what was thought to be a soft chancre. At that time the glands were removed from the inguinal regions on both sides. From time to time the patient had swellings of the penis and scrotum, which always subsided without treatment. Nine weeks before he came to the clinic a swelling of the penis and scrotum suddenly developed and persisted. The Frei reaction was strongly positive. Serologic reactions and tests for a previous infection with Ducrey's bacillus were negative. A portion of the edematous skin was removed, and two weeks later there were lymph fistulas. Six months later abscesses appeared in the scrotum and groin. The histologic changes in the elephantiasic tissue were similar to those which are observed in the lymph glands in cases of lymphogranuloma venereum and in tissues in the presence of the anorectal syndrome. The authors felt that blockage of the flow of lymph by changes in the glands was not sufficient to cause the elephantiasis but that specific inflammatory changes seen in the peripheral lymph vessels added to the obstruction of lymph flow in the genitalia. They believed that recanalization of thrombosed lymph vessels accounted for the early spontaneous disappearance of the edema in their case.

16 Barthels, C., and Biberstein, H. Elephantiasis penis et scroti und Lymphogranulomatosis inguinalis, Beitr. z. klin. Chir. 152 325-338, 1931.

They suggested that the virus of lymphogranuloma venereum varies in virulence from time to time and that it may remain in the tissues in a latent state

Stryker and Ploch¹⁷ were the first in the United States to report a case of elephantiasis of the penis and scrotum in which lymphogranuloma venereum was the etiologic agent

Navarro Martin¹⁸ reported a case of lymphogranulomatous elephantiasis of the penis and scrotum with concomitant stricture of the rectum Cole¹ observed a similar case Equally significant are the observations of de Gregorio,¹⁹ who reported a case of elephantiasis of the penis due to a chronic lymphogranulomatous ulcer in the balanopreputial region This patient's wife became infected and later had rectal stenosis

Coutts and Ahumada²⁰ reviewed the literature pertaining to the cutaneous manifestations of lymphogranuloma venereum and reported a case, describing an unusual lymphogranulomatous syndrome A man aged 36 who had previously contracted syphilis and gonorrhea later had a slight urethral discharge which subsided without treatment At about the same time the genitalia began to enlarge Within six months the penis and scrotum were considerably increased in size and squamous lesions began to appear on the legs and gluteal regions The cutaneous lesions eventually became large psoriasiform plaques, and in certain areas ulcerations appeared which simulated ecthyma

The Wassermann reaction, the lymphatic reaction and the Kahn reaction were positive The intradermal Frei test gave a negative reaction, but an antigen prepared from the cutaneous lesions gave a positive reaction in patients with lymphogranulomatous syndromes and a negative reaction in healthy controls No statement was made regarding the effect of antisyphilitic treatment on the cutaneous lesions or the elephantiasis of the genitalia

17 Stryker, G V, and Ploch, B Elephantiasis of Penis and Scrotum A Sequela of Lymphogranuloma Inguinale, Arch Dermat & Syph **32** 86-89 (July) 1935

18 Navarro Martin, A Elefantiasis peneoescroftal de origen linfogranulomatoso, Actas dermo-sif **27** 425-430 (Jan) 1935

19 de Gregorio, E Ulcération chronique et éléphantiasis de la verge et stenose rectale conjugale dans la maladie de Nicolas-Favre, Rev franç de dermat et de vénéréol **12** 259-271 (May) 1936

20 Coutts, W E, and Ahumada, H Penoscrotal Elephantiasis of Lymphogranulomatous Origin Description of a Case with Psoriasiform Cutaneous Lesions and Others Resembling Ecthymatous Pyoderma, Arch Dermat & Syph **36** 1014-1017 (Nov) 1937

In a review of this case, Wise and Sulzberger²¹ raised the question of positive anergy as an explanation for the negative Frei reaction of this patient

A few more cases of elephantiasis of the male genitalia caused by lymphogranuloma venereum have been reported (Coutts and Herrera,²² Nicolas, Lebeuf and Charpy,²³ Vigne, Bonnet and Lombard²⁴

It is well known that in lymphogranuloma venereum there is a great discrepancy in the incidence of suppuration of the inguinal lymph nodes, the anorectal syndrome and elephantiasis of the genitalia in men and women. The reason for this variance is the difference in the lymphatic circulation of the genitalia, the anus and the rectum in the male and in the female. This fact has been adequately discussed by Barthels and Biberstein,²⁵ Cole,¹ Bloom²⁶ and others, therefore we have omitted a description of these anatomic differences

REPORT OF A CASE

A white man aged 60 came to the clinic on Nov 17, 1937, complaining of an enlargement of the penis and scrotum. The family history and marital history were unimportant. The patient had had typhoid fever at the age of 30 and eight years later had contracted malaria while serving with the army in the Philippine Islands. At this time he suffered an attack of jaundice. He continued to have about one attack of "chills and fever" every year. For years he drank alcoholic beverages to excess, but in recent months he had been more temperate. He denied having had gonorrhea but stated that at the age of 25 he had a sore on the penis. This lesion was cauterized and disappeared within two weeks. He was certain that a generalized eruption did not develop, but he did have a suppuration of the inguinal lymph nodes on the right with subsequent sinus formation lasting several weeks. He had never received antisyphilitic treatment, and recent Wassermann reactions were reported to have been negative.

21 Wise, F, and Sulzberger, M B. Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc, 1938, p 372

22 Coutts, W E, and Martini Herrera, J. Elephantiasis penis et scroti in ihrer Beziehung zur Lymphogranulomatosis venerea, Dermat Wchnschr **98** 784-785 (June 23) 1934

23 Nicolas, J, Lebeuf, F, and Charpy, J. Elephantiasis genital chez un malade opéré, il y a 18 mois, pour maladie de Nicolas-Favre. Etude des intradermoreactions, Bull Soc franç de dermat et syph **39** 27-28 (Jan) 1932

24 Vigne, P, Bonnet, J, and Lombard, R. Elephantiasis de la verge consecutif a un evidentement ganglionnaire bilateral ancien pour maladie de Nicolas-Favre, Marseille-med **1** 463-465 (April 25) 1937

25 Barthels, C, and Biberstein, H. Zur Aetiologie der "entzündlichen" Rektumstrikturen (Lymphogranulomatosis inguinalis als Grundkrankheit), Beitr z klin Chir **152** 161-183, 1931

26 Bloom, D. Strictures of the Rectum Due to Lymphogranuloma Inguinale, Surg, Gynec & Obst **58** 827-840 (May) 1934

The present illness began about 1928. The initial manifestation consisted of moderate thickening of the scrotum accompanied by mild pruritus. These changes were of minor importance until two years later, when suddenly the penis and scrotum greatly increased in size. There were no concomitant lesions of the genitocrural region that could have been considered as a cause for the enlargement of the genitalia. On the day before the sudden changes occurred the patient lifted a very heavy object, consequently, he attributed his difficulty to the strain. During the past seven years there had been no decrease in the size of the genitalia.



Fig 2 (case 3) —Elephantiasis of the penis and scrotum

The subjective symptoms disappeared with the onset of elephantiasis. Coitus was impossible, and the patient had been impotent for the past seven years (fig 2).

With the exception of enlargement of the genitalia, physical examination showed only a few minor abnormalities. There was a slight impairment of hearing, and the sclerae were yellowish. Many teeth were carious, and there was chronic gingivitis. The liver was not palpable. Roentgen examination of the chest, gastrointestinal tract and genitourinary system revealed no abnormality. The prostate was moderately enlarged.

The most striking abnormality was enlargement of the genitalia. The scrotum was about the size of a small grapefruit, and the penis was correspondingly



Fig 3 (case 3)—Section from the scrotum, showing edema, dilatation of vessels and hypertrophy and hyperplasia of connective tissue, $\times 150$

enlarged The scrotum, the prepuce and the skin of the penis were edematous Firm digital pressure produced slight pitting The normal cutaneous markings were accentuated, but there were no lymph vesicles or verrucous papules on the scrotum or on the penis The color of the scrotum varied only slightly from normal, except in the more dependent portion, which was dull pinkish blue There were no discharging sinuses and no urethral discharge The glans penis could not be exposed The testicles were apparently of normal size There was a scar in the right inguinal region

The routine blood cell and differential counts were normal The sedimentation rate was 0.76 mm per minute The icterus index was 20 units A red blood cell fragility test showed beginning hemolysis at 0.55 per cent and complete hemolysis at 0.38 per cent The value for serum protein was 5.3 Gm per hundred cubic centimeters (albumin 4.1 Gm, globulin, 1.2 Gm) The Wassermann and Kahn reactions were negative The spinal fluid was normal Repeated examinations for filaria and plasmodia gave negative results Bromsulphalein and Takata-Ara tests indicated a slight impairment of hepatic function The Frei reaction was strongly positive

Dr E. Perry McCullagh of the department of endocrinology made studies to determine whether the prolonged insulation of the testicles by the greatly thickened scrotum had altered the gonadal function An assay for estrogen showed 20 to 30 rat units per daily output of urine (normal, 30 to 60 units) The Friedman test showed slight traces of gonadotropic hormone, and a quantitative assay for androgenic substance showed 169 international units (normal, 20 to 80 units)

Histologic Examination—Tissue for histologic examination was removed from the right side of the scrotum

Epidermis Changes in the corium had obliterated most of the papillae and had reduced the epidermis to five or six layers of cells The surface of the epidermis was covered by a thin hyperkeratotic layer There was no parakeratosis The granular layer consisted of one layer of cells The rete mucosum showed moderate intercellular edema, and the basal layer was intact (fig. 3)

Corium There was an enormous increase in thickness of the corium There were diffuse edema and great hypertrophy and hyperplasia of the connective tissue These changes extended into the subcutaneous tissue The edema was most marked in the upper part of the corium The blood and lymph vessels in the papillary and subpapillary layers were greatly dilated Perivascular edema was most prominent about the larger vessels There were few areas of cellular infiltration, however, fibroblasts and numerous connective tissue nuclei were scattered throughout the corium The fibers of the dartos were edematous and stained poorly, and in many places the cytoplasm had disappeared, leaving deeply stained nuclei surrounded by clear spaces This degeneration and final vacuolization were more marked in some muscle bundles than in others (fig. 4)

In the lower portion of the section and in the dense trabeculae of the dartos there were a few small, well circumscribed areas of closely packed small lymphocytes There were no giant cells or areas of cellular infiltration of a granulomatous type The sweat and sebaceous glands were sparse but normal

Diagnosis—A diagnosis of cirrhosis of the liver and congenital hemolytic jaundice was made by Dr Russell L. Haden The enlargement of the genitalia was considered to be a manifestation of lymphogranuloma venereum



Fig 4 (case 3) —Dilatation of an arteriole, perivascular edema and an area of lymphocytic infiltration in the deeper portion of the corium, $\times 600$

COMMENT

The cases presented here are examples of a rare and unusual elephantiasis. Elephantiasis of the scrotum from any cause is an unusual condition, and judging from the scarcity of reports during the past three decades the elephantiasic enlargement of the lip which was observed in our cases is almost a forgotten entity. The rolled-out, doughy, elastic, diffuse, symptomless enlargement of the lips occurring without preceding acute cellulitis and without enlargement of the regional lymph glands or distortion of the normal form of the lip constitutes a condition of which there is no counterpart.

Although this condition has been reported as occurring only in syphilitic persons, there is reason to doubt that syphilis is the true cause. The rarity of the disease precludes an extensive investigation of this problem by a single observer. All observers have based their opinions regarding the nature of Fournier's diffuse hypertrophic syphiloma on clinical findings. So far as we have been able to determine, no one has studied the pathologic character of this condition, and until some one is able to obtain tissue for histologic examination the nature of the hypertrophy will remain obscure. We deeply regret our inability to obtain the permission of our second patient for a biopsy and also realize that our failure to do a Frei test somewhat decreases the value of this report. However, a positive Frei reaction would only have indicated the coexistence of syphilis and lymphogranuloma venereum and could not have been considered conclusive proof that the enlargement of the lip was of lymphogranulomatous origin. A study of the histologic changes in the lip would have been of greater importance.

Is the elephantiasis of the lip in these cases of syphilitic origin? If not, is there any reason to suspect that, as in some cases of elephantiasis of the genitalia, lymphogranuloma venereum may be the cause? The only approach to this problem is to attempt to correlate certain significant features of the cases that have been reported with the present concept of lymphogranuloma venereum and elephantiasis.

In all of the cases which we have reviewed, the enlarged lip was soft, elastic and free of palpable infiltration. These characteristics are not compatible with the presence of gummatous infiltration. Also, it is significant that while the enlargement of the lip remained unchanged, the concomitant mucocutaneous manifestations of late syphilis responded favorably and promptly to antisyphilitic treatment. We are cognizant that in rare cases a gummatous lesion fails to respond favorably to antisyphilitic therapy; however, in such cases any coexisting late syphilid is likewise resistant to treatment. In view of these facts we feel that there is reason to doubt seriously the syphilitic origin of Fournier's diffuse hypertrophic syphiloma.

Although we are without substantial evidence, we feel that there is sufficient reason for suspecting that this type of elephantiasis of the lip may be caused by lymphogranuloma venereum. Syphilis and lymphogranuloma venereum are usually of venereal origin and are frequently coexisting infections. Some patients with esthiomene and the anorectal syndrome have had both diseases, and, although concomitant manifestations of syphilis disappeared under antisyphilitic treatment, the elephantiasis of the vulva and rectal stenosis remained unchanged. Identical observations have been reported in cases of elephantiasis of the penis and scrotum of probable lymphogranulomatous origin. Of particular interest is the case reported by Whitfield, in which enlargement of the lips was preceded by elephantiasis of the genitalia of unexplained origin. The concomitant syphilids disappeared under antisyphilitic treatment, but the elephantiasis was altered only slightly. The case reported by Weidman and Hunter, in which chronic edema of the eyelids, penis and scrotum occurred in a patient with lymphogranuloma venereum, should be cited as additional presumptive clinical evidence of the lymphogranulomatous origin of certain elephantiasic conditions of the lips, face and eyelids.

The clinical characteristics of diffuse hypertrophic syphiloma and of lymphogranulomatous elephantiasis of the penis and scrotum are similar. In both conditions there is usually a history of a venereal infection several years prior to the onset of elephantiasis. The enlargement begins insidiously without any apparent cause and frequently progresses suddenly to a certain point, remaining unchanged for several years. The elastic, symptomless, nonpitting edema is similar in the two conditions.

Barthels and Biberstein's observations indicate that the virus of lymphogranuloma venereum may remain dormant in the tissues and when activated may produce lymphangitis and lymph stasis which may terminate in elephantiasis. Since lymphogranuloma venereum is a systemic infection, it is not unreasonable to believe that such changes may be incited by this virus in portions of the body remote from the genitalia and the rectum.

We believe that there are good reasons for doubting the syphilitic origin of the diffuse hypertrophic syphiloma of Fournier and that it is probable that future investigations will show this condition to be a rare manifestation of lymphogranuloma venereum.

A review of the literature shows that syphilis is rarely the chief etiologic factor in elephantiasis of the male genitalia. Undoubtedly, in many cases which have been reported as examples of syphilitic elephantiasis of the penis and scrotum the condition was in reality of lymphogranulomatous origin. In case 3 there was a strongly positive

Frei reaction and a history of venereal disease which was compatible with the diagnosis of lymphogranuloma venereum. Also, we were unable to demonstrate any other probable etiologic agents. This case was identical with the one reported by Barthels and Biberstein and others. The difference between the histologic changes in case 3 and in the cases reported by Barthels and Biberstein may be explained by the fact that the elephantiasis in our case had remained unchanged for seven years before a biopsy was performed. The virus in the scrotal tissue was in a latent state.

SUMMARY AND CONCLUSIONS

A critical review of the literature shows that syphilis is rarely the sole cause in elephantiasis. In many cases reported as examples of syphilitic elephantiasis, secondary streptococcic lymphangitis was probably the chief cause of the condition, in others the elephantiasis was coincidental with an existing syphilitic infection.

Two cases of the rare and almost forgotten syndrome described by Fournier under the title of diffuse hypertrophic syphiloma are reported.

The importance of syphilis and lymphogranuloma venereum as possible causes of elephantiasis of the lip and of the male genitalia is discussed.

A case of elephantiasis of the penis and scrotum in which the probable cause was lymphogranuloma venereum is reported.

ABSTRACT OF DISCUSSION

DR HAROLD N. COLE, Cleveland. I had the opportunity to see 1 of these patients. I think Trimble wrote something on the subject of elephantiasis of the lip in connection with syphilis. In regard to elephantiasis of the genitalia, in the past year or so I studied several more patients, and in 1 patient I was unable to prove the existence of lymphogranuloma venereum but was able to find Donovan bodies in the tissue, I therefore felt that the condition was probably granuloma inguinale. I am a little more conservative, therefore, about the theory that this type of elephantiasis is caused only by lymphogranuloma venereum.

DR E. W. NETHERTON, Cleveland. I had hoped to point out that there is a definite clinical similarity between the cases of elephantiasis of the lip of the type just discussed and those of elephantiasis of the genitalia. Some cases have been reported in which the elephantiasis of the genitalia preceded the elephantiasis of the lip. We believe that it is probable that future observations of thoroughly studied cases of elephantiasis of the face involving the eyelids and lips will show that in some cases of the type which have heretofore been thought of as syphilitic elephantiasis the elephantiasis is another manifestation of lymphogranuloma venereum.

A SIMPLIFIED COMPLEMENT FIXATION TECHNIC FOR THE DIAGNOSIS AND TREATMENT OF SYPHILIS

ITS SENSITIVITY AND SPECIFICITY

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AND

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Recently two of us¹ described a simplified complement fixation technic for syphilis, the advantages of which include reduction in time and labor, cost and technical errors. Without any loss of specificity, it showed an increased sensitivity over the routine Kolmer modification of the Wassermann test. Preliminary comparisons have also shown it to be more sensitive than the Kahn precipitation test, although less so than the Eagle test. It is now being used at the Graduate Hospital as one of three routine tests on all serums, the other two being the Kahn and the Eagle precipitation test.

A careful record of the results in a series of 1,500 tests (of both syphilitic and nonsyphilitic patients) has furnished us with additional data relative to its significance in the diagnosis of syphilis and the exclusion of syphilis both in patients from the syphilis service and in those admitted to the hospital at large. In all instances the Kahn and the Eagle test were performed on identical serums.

Any advance in the simplicity or sensitivity of the Wassermann test should be welcomed, as it is our feeling that for the diagnosis of syphilis a battery of three tests should be used when possible, with a complement fixation test as one of the three. When two tests are in disagreement,

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1 Boerner, F., and Lukens, M. (a) A Simplified Complement Fixation Technic for the Serologic Diagnosis of Syphilis, *Am J Clin Path* 9 13, 1939, (b) A Study of the Sensitivity and Specificity of the Simplified Complement Fixation Test for Syphilis, to be published.

as happens not infrequently, the third test becomes of extreme usefulness, if only as a referee. In this report, we shall refer to our modification of the complement fixation test as the B-L modification.

TECHNIC

The technics of the Kahn and the Eagle test were outlined by their originators.² The B-L modification differs from the other modifications of the Wassermann test particularly in the mixing of certain of the reagents in bulk and the use of optimum doses of complement, hemolysin and antigen in place of units. Antigen and complement are combined and added as a single increment to the patient's serum, and then sensitized sheep cells are added. All reagents are used in smaller amounts, i. e., 0.1 cc of serum is used, 0.5 cc of antigen-complement and 0.5 cc of sensitized cells. The total is but slightly over 1 cc. The amount of serum used, however, is really equal to or greater in relation to the reagents than the 0.2 cc of serum that we have previously used in the Kolmer modification. Ice box fixation and

TABLE 1—*Boerner-Lukens Modification of the Complement Fixation Test (Qualitative)*

| | Serum,
Cc | | Antigen-
Complement
Mixture,
Cc | Complement
1.30,
Cc | | Sensitized
Cells
(0.75%),
Cc | | Results |
|-----------------------|--------------|---------|--|---------------------------|---|---------------------------------------|---------|--------------|
| Tube 1 | 0.1 | 10 min | 0.5 | | 15 to 18 hours | 0.5 | 1 hour | |
| Tube 2 | 0.1 | at 58 C | | 0.5 | at 8 to 10 C,
followed
by 10 min
at 37 C | 0.5 | at 37 C | |
| Antigen
control | 0.1* | | 0.5 | | | 0.5 | | Hemolysis |
| Complement
control | | | | 0.5 | | 0.5 | | Hemolysis |
| Corpuscle
control | 0.5† | | | | | 0.5 | | No hemolysis |

* Normal serum

† Saline

incubation of the mixture are essentially the same as in other modifications. Concerning the reagents and their titration, adjustment and preservation, detailed description has been given in a previous publication.^{1a} Actually there are but three additions of reagents, the absence of any being readily detected by the difference in resultant volume. This makes for simplicity and ease of performance as well as of supervision. Although the volume is approximately one-third that used in the usual Wassermann test, the result is read with extreme ease in either Kolmer or Kahn tubes. The antigen used is prepared by a simplified method described by two of us in collaboration with Jones.³ It is fortified with 0.4 per cent cholesterol, and its preparation requires but a few hours.

In this series, all reactions were read as positive, doubtful or negative, in accordance with the recommendations of the Committee on the Evaluation of Serologic Tests for Syphilis. In the complement fixation tests, only results usually

2 Kolmer, J. A., and Boerner, F. *Approved Laboratory Technic*, ed 2, New York, D. Appleton-Century Company, Inc., 1939.

3 Boerner, F., Jones, C. A., and Lukens, M. A Simplified Method for the Preparation of an Antigen for Use in the Complement Fixation Test for Syphilis, *Am J Clin Path* 9:321, 1939.

denominated as 4 plus were called positive. Results of 3 plus, 2 plus, 1 plus and plus over minus were reported as doubtful, and complete hemolysis as negative. The Kahn test was reported according to the recommendation of Kahn, namely, a count over 6 as positive, from 2 to 5½ as doubtful and less than 2 as negative.

SENSITIVITY

From the data in table 2 it is apparent that the B-L modification of the Wassermann test is decidedly more sensitive than the Kahn test, but less sensitive than the Eagle test. These findings confirm a previous similar study by two of us.^{1b} The proportionately larger number of doubtful Kahn tests is likely due to conservatism in the arbitrary division

TABLE 2—*Results of Tests on 1,500 Serums*

| B L Modification | | Kahn Test | | Eagle Test | |
|------------------|-------|-----------|-------|----------------------------------|----------------|
| Positive | 396 | Positive | 148 | Positive | 148 |
| | | Doubtful | 87 | Positive
Negative | 84
3 |
| | | Negative | 161 | Positive
Doubtful
Negative | 151
1
9 |
| Doubtful | 46 | Positive | 1 | Positive | 1 |
| | | Doubtful | 15 | Positive
Doubtful | 14
1 |
| | | Negative | 30 | Positive
Negative | 23
7 |
| Negative | 1,058 | Positive | 2 | Positive
Negative | 1
1 |
| | | Doubtful | 24 | Positive
Negative | 16
8 |
| | | Negative | 1,032 | Positive
Doubtful
Negative | 60
1
971 |

into positive and doubtful readings. This belief is supported by the fact that of 126 serums giving a doubtful Kahn reaction only 8 reacted negatively by both the B-L modification and the Eagle test. For the purpose of adequate comparison of the sensitivity of the tests, we believe that the positive and doubtful reactions should be grouped together. A doubtful reaction as interpreted by us usually is indicative of syphilis, except when it is refuted by the other two tests or is without confirmation on repetition.

SPECIFICITY

It was not possible to follow all cases in which the reaction was positive. Therefore, we directed our attention to those instances of positive B-L reactions associated with negative Kahn and Eagle reactions. It appeared reasonable that an analysis of this group would be most likely to reveal any false positive reactions. There were 9

cases in which such results were obtained and 4 of a positive reaction to the B-L test and a doubtful reaction to either the Eagle or the Kahn test. A résumé of these cases is given in table 3.

TABLE 3—*Résumé of Thirteen Cases of "Positive" B-L Tests*

| Case No | Description of Patient | | | Diagnosis | Comment |
|----------------|--|---|-----|---|--|
| | Race | Sex | Age | | |
| | a | Nine Cases of "Negative" Kahn and Eagle Tests | | | |
| 1, 2, 3, 4 | | | | Under treatment for syphilis | |
| 5 | White | ♂ | 33 | Patchy atrophic gastritis | Still under study, subsequent Kahn and Eagle test "doubtful" |
| 6 | Negro | ♀ | 46 | Former thyrotoxicosis, present cholelithiasis | Dilated aorta, aortic second sound accentuated, test repeated with same result |
| 7-8 | | | | For blood bank | Impossible to follow up to date |
| 9 | . | | | | False result, technical error |
| | b | Three Cases of "Doubtful" Kahn and "Negative" Eagle Tests | | | |
| 10 11 | | | | Under treatment for early syphilis | |
| 12 | | | | | Transient false positive |
| | c | One Case of "Negative" Kahn and "Doubtful" Eagle Tests | | | |
| 13 | | | | Under treatment for late syphilis | |
| Recapitulation | 7 patients under treatment, 1 patient suspected of syphilis, 3 patients incompletely studied, and 2 patients with false positive reactions | | | | |

TABLE 4—*Résumé of Seven Cases of "Doubtful" B-L Test with "Negative" Kahn and Eagle Tests*

| Case No | Description of Patient | | | Diagnosis | Comment |
|----------------|---|-----|-----|-------------------------------------|---|
| | Race | Sex | Age | | |
| No 1 with 3+ | White | ♂ | 53 | Diabetes, lobar pneumonia | Febrile, light reflexes and deep tendon reflexes lost, serologic tests not repeated |
| No 2 with 2+ | Negro | ♀ | 34 | Pyonephritis | Febrile, sluggish pupils, serologic tests not repeated |
| No 3 with 2+ | White | ♀ | 35 | Rectal stricture, rectovaginal mass | Single serologic test, examination incomplete |
| No 4 with 2+ | Negro | ♂ | | Treated syphilis | |
| No 5 with 1+ | White | ♀ | 25 | Chronic bronchitis | False doubtful reaction, technical error |
| No 6 with 1+ | White | ♀ | 23 | Lobar pneumonia | Febrile |
| No 7 with ± | Negro | ♂ | 56 | Lumbar sacral strain | Pupils unequal and sluggish to light, deep reflexes absent, further study needed |
| Recapitulation | 1 patient under treatment, 1 patient suspected of syphilis, 4 patients incompletely studied, and 1 patient with false doubtful reaction | | | | |

There were 7 cases of doubtful positive reaction to the B-L test and negative reactions to both the Kahn and the Eagle test. A résumé of these cases is given in table 4.

In the 16 cases in which the B-L modification of the Wassermann test was the only one eliciting a reaction, there were 2 false positive

reactions, 1 false doubtful reaction and 7 reactions that could not be satisfactorily evaluated. At least 1 of the false positive reactions was discovered by retesting, and thereby a false report was avoided.

COMMENT

One is tempted to restate or formulate a sort of decalogue by which the physician should be guided. The truisms expressed are far from unique with us but deserve reemphasis, as confirmed by our experience and investigations.

1 For the routine serologic evaluation of syphilis at least two tests should be employed: one a complement fixation and the other a flocculation test. Ideally, three tests would be an improvement, the third acting in the capacity of referee.

2 A single positive report, even though all tests on the same serum give a strong positive reaction, should never be sufficient for the diagnosis of syphilis in the absence of clinical symptoms.

3 In the absence of clinical symptoms a positive reaction should be followed by a second test after a week.

4 All tests for routine diagnosis might well be reported as "positive," "doubtful" or "negative."

5 However, for patients to be treated or under treatment, the report of the test should indicate the degree of positivity.

6 A doubtful reaction to one test is more significant when accompanied with a positive reaction to the other or others and may be considered positive.

7 In all cases clinically early syphilis with positive serologic reports may be considered syphilis and treated immediately.

8 All serologic reports should indicate the tests employed and any modifications thereof.

9 A report of a negative serologic reaction (by any test) can never be taken as proving the absence of syphilis.

10 Reliance cannot be placed on serologic tests performed during an acute infectious or febrile stage of any disease.

SUMMARY AND CONCLUSION

We have described a new modification of the complement fixation test for syphilis, which has been determined to be more sensitive than the Kolmer modification and the Kahn flocculation test, although less so than the Eagle flocculation test. There has been no loss in specificity.

The Boerner-Lukens modification of the complement fixation test tends toward simplification through the use of an easily prepared

antigen and the addition of the reagents in combination. There ensues less labor and cost and the addition of improved supervision

In a series of 1,500 tests, there were 20 instances of lack of accord in specificity, all of which are analyzed against the clinical status of the patient

The continuance of the use of two or three tests for the serologic evaluation of syphilis is urgent

A closer rapport is necessary between the serologist and the clinician, in order that the patient's interests may best be served

EFFECT OF BISMUTH THERAPY ON LATENT PLUMBISM

PRELIMINARY REPORT

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In comparison with the arsenicals and mercurials employed in the treatment of syphilis, the bismuth preparations show a notably low toxicity. Stomatitis constitutes the only commonly encountered complication following the intramuscular injection of bismuth salts. Other reactions, including arterial and venous embolism, abscesses, arthralgia, jaundice, nephritis and cutaneous lesions, are rarely seen.

Stokes¹ listed such disturbances as abdominal cramps, diarrhea, polyneuritis, psychic symptoms and erythropoietic disturbances as following the administration of bismuth in the treatment of syphilis. These are also regularly noted in lead poisoning. This communication suggests that some of these reactions reported as being due to bismuth may actually have been the result of lead toxicity. Bismuth and lead are closely related chemical elements, and there is no reason why the toxicology of one should not resemble the toxicology of the other to a certain extent. However, latent plumbism is commonly encountered, especially in industrial centers, while bismuth toxemia is comparatively uncommon. The following case reports show that latent plumbism may become active after the injection of bismuth as an antisyphilitic agent.

REPORT OF CASES

CASE 1—G L M, a 27 year old white man, was employed in a lead smelter in Idaho from January to June 1936. He stated that while he observed all possible precautions, such symptoms as abdominal and muscular cramps, discoloration of the gums, weakness and shortness of breath developed, and eventually he fainted while at work. The air in the smelter was said to have been saturated with lead dust. He was hospitalized in Kellogg, Idaho, for five weeks. A diagnosis of lead poisoning was made at this time. During the ensuing seven months he attempted to return to work on several occasions but each time suffered recurrences of the same symptoms. He finally abandoned the idea of continuing this line of employment. During his illness he lost 22 pounds (10 Kg.)

After this he was well until April 15, 1939, when a urethral discharge developed. This was diagnosed at a camp in California as gonorrhea and was treated accordingly. Early in June he noted four papular lesions on his penis, and a diagnosis of secondary syphilis was made and confirmed by serologic tests of the blood.

¹ Stokes, J H. Modern Clinical Syphilology, ed 2, Philadelphia, W B Saunders Company, 1934

Antisymphilitic therapy was instituted at the camp by the simultaneous injection of 0.06 Gm of mapharsen and 0.13 Gm of bismuth subsalicylate. He received four injections of each within ten days. After this he was given three additional injections of each at weekly intervals.

The patient noted a recurrence of abdominal and muscular cramps, discoloration of the gums and weakness after the second treatment. These symptoms increased in severity after each subsequent injection. In addition, he lost 12 pounds (5.5 Kg.), in contradistinction to the gain in weight usually experienced by patients with early syphilis after the institution of therapy. His symptoms usually became aggravated twelve to twenty-four hours after the injections, although they were usually present constantly. He also complained of decreasing vision in his right eye. Examination revealed a typical lead line, consisting of pinpoint bluish black spots, less than 1 mm from the gingival margin. The patient claimed that this had started only since the beginning of the injection therapy. The gums were not diffusely discolored as in bismuth pigmentation.

Bismuth therapy was discontinued, but the patient continued to receive intravenous injections of mapharsen. Within two weeks most of his symptoms, including the decrease in vision and the lead line, were greatly improved. Two weeks later he reported that he was entirely well.

CASE 2—S. T., a 34 year old painter, stated that in September 1937 several lesions developed on his tongue and on his right thenar eminence. He visited a general practitioner, who found serologic evidence of syphilis in the patient and initiated therapy consisting of the intravenous injection of neoarsphenamine every five days. After twelve such treatments had been given, bismuth therapy was instituted.

After the first intragluteal injection, the patient suffered a sore hip and refused further treatments in this location. Therefore, he was given an injection of bismuth subsalicylate every five days in the left deltoid muscle. Soreness here did not inconvenience him at his work. In December 1937, after two or three such injections, the patient became very ill and was hospitalized. At this time he suffered severe abdominal cramps, pigmentation of the gums and other signs and symptoms leading to the diagnosis of lead poisoning. He remained in the hospital for about one month. After this, antisymphilitic therapy was resumed and he received 0.6 Gm of neoarsphenamine every five days until I first saw him, on June 22, 1938.

Physical and laboratory examinations at this time gave completely negative results. He was given one injection of bismuth subsalicylate in the right hip, and because of a certain amount of soreness he refused further intragluteal therapy. As a result, the next two injections were administered into the left triceps muscle.

After the third treatment, the patient experienced severe abdominal cramps that he thought were like those he had suffered the previous December. Examination showed a number of discrete pinpoint pigmented spots on the side of the tongue about 1 mm from the gingival margin. Bismuth therapy was immediately discontinued, but the patient continued to have severe intermittent abdominal pains for the following five weeks.

Since then he has received no further bismuth therapy, and there has been no recurrence of these signs or symptoms, despite his continuing to work as a painter.

COMMENT

Antisymphilitic therapy must be as nearly reactionless as possible to be successful. Not even financial considerations will lead to lapses in treatment as regularly as unpleasant paratherapeutic incidents. Con-

sideration of the cases reported here may explain some of the so-called "bismuth intolerances" and allow physicians to smooth the therapeutic road further

It has been amply proved that lead is stored in the skeletal system of the body. In this location it is believed to be innocuous. However, when the stored metal is mobilized, or in other words when it is removed from the bones and taken into the circulation, a characteristic group of symptoms appear. This, of course, occurs when the amount of lead in the blood exceeds the concentration that the body can tolerate. These symptoms include pigmentation near the gingival margin, abdominal cramps, constipation or diarrhea, peripheral neuritis, anemia, stippling of the erythrocytes, encephalopathies and other derangements.

This mobilization may be accomplished in many ways. As simple a factor as an acid diet may be all that is necessary. Roentgenographic studies have shown that a lead line may be demonstrated near the epiphyses of growing children suffering from lead poisoning. A similar line has been found after bismuth therapy, and the consensus is that these lines are radiologically indistinguishable. This suggests that the two metals are stored in the same location. Fishback and Fishback² have demonstrated that after antisyphilitic therapy the greatest amount of mobile bismuth is found in the bones.

It is possible that the deposition of bismuth in the osseous system leads to the excretion of lead and explains the development of signs and symptoms of lead poisoning in such patients. These manifestations are dependent on the amount of lead in the circulation and not on the total amount present within the body.

A survey of the occupations in which the worker is exposed to lead suggests that latent plumbism must be common. According to Solis-Cohen and Githens³ the exposed workers include painters, lead miners, lead workers, plumbers, type setters, dye workers, storage battery builders or repairers, enamelers, bullet makers, pottery glazers, paint manufacturers, solder handlers and gasoline (tetra-ethyl lead) handlers. Under these circumstances it is not surprising that bismuth therapy should occasionally cause activation of latent lead poisoning if the mechanisms suggested in this communication are correct.

The diagnosis of plumbism in these patients is based entirely on clinical evidence, but a careful consideration of the observations leaves little or no doubt as to its correctness. Both patients were exposed to lead. One was exposed during the treatments, and the other had had definite lead poisoning before receiving any bismuth therapy. One patient presented pinpoint pigmented spots on his tongue, which are

² Fishback, H. R., and Fishback, D. Experimental Studies of Long Continued Administration of Bismuth, *J. Lab. & Clin. Med.* **23** 127 (Nov.) 1937.

³ Solis-Cohen, S., and Githens, T. S. Pharmacotherapeutics, *Materia Medica and Drug Action*, New York, D. Appleton and Company, 1928.

seen in lead poisoning but are of questionable occurrence in bismuth toxemia. The pigmentation of the gums was localized rather than diffuse, as commonly encountered after the injection of bismuth salts. The abdominal cramps experienced by these patients were much more severe than any personally observed as the result of administration of bismuth. Exactly the same symptoms developed in the first patient (case 1) after the injections of bismuth subsalicylate as those he had had during his previous attack of classic chronic lead poisoning. Case 2 was presented before the San Francisco Dermatological Society,⁴ and the general tenor of the discussion was in agreement with the views expressed in this paper.

The second patient (case 2) was admittedly lax in removing the paint from his skin and clothes. This undoubtedly added to the amount of lead absorbed, increasing the need for storage space over the amount required by a cleanly worker. The daily ingestion of two quarts of milk was insufficient to prevent the development of manifestations of plumbism while this patient was receiving bismuth therapy. Since the cessation of injections of the bismuth compound he has been able to continue working as a painter without difficulty. Unfortunately neither patient was sufficiently cooperative to allow experimentation with various preparations, including bismuth and mercurials (orally administered), calcium, ascorbic acid and sodium thiosulfate.

This complication is apparently seldom recognized, as discussion of the matter with other dermatologists has failed to reveal a similar case. However, its potential importance is obvious when one considers the large number of patients who are constantly exposed to the noxious effects of lead. Therefore, it is suggested that the prophylactic treatment of lead poisoning in such workers as painters who are being given injections of bismuth preparations might further decrease the incidence of therapeutic complications in the treatment of syphilis.

SUMMARY

The cases of a painter and a smelter worker are presented. Signs and symptoms of lead poisoning in both patients followed the administration of bismuth in the treatment of a syphilitic infection.

It is suggested that bismuth may replace the lead stored in the bones and lead to the mobilization of lead, with the development of such symptoms as cramps and a lead line.

Prophylactic treatment of lead poisoning in those exposed to the influence of the metal may decrease the incidence of untoward reactions following bismuth therapy.

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⁴ Epstein, E: Intolerance to Heavy Metal, *Arch. Dermat. & Syph.* 39:570 (March) 1939.

LXXXVII—CHROMOMYCOSIS OF THE FACE

REPORT OF A CASE AND A STUDY OF THE CAUSATIVE ORGANISM,
PHIALOPHORA VERRUCOSA

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Resident in Dermatology

ST LOUIS

Chromomycosis (chromoblastomycosis), or dermatitis verrucosa, is a disease which has received little attention until recently, because of the small number of cases. Clinically it is a dermatitis usually of the extremities (hands or feet), which may be papular, nodular, verrucoid or granulomatous, with or without ulceration and abscess formation and usually yellowish brown. There has been no report of a systemic invasion, lymphangitis, pain or pruritus except in 1 case¹. The microscopic picture may resemble that of tuberculosis, sporotrichosis, blastomycosis, syphilis, a granuloma or a foreign body reaction. However, brown thick-walled cells are seen in the tissue, probably chlamydospores, with intracellular wall formation and no budding. These structures are usually seen within the abscesses or giant cells.

The almost regular occurrence of the process on the extremities makes a lesion on any other part of the body seem unusual. With the exception of the first case reported in the United States by Lane² and by Medlar,³ in which the lesions occurred on the buttock, and the one reported by Pedroso and Gomes⁴ in Brazil, in which a lesion secondary

Studies, observations and reports from the Departments of Dermatology and Mycology of the Barnard Free Skin and Cancer Hospital, service of Dr M F Engman, Sr

1 Carrion, A L, and Koppisch, E. Observations on Dermatomycosis in Puerto Rico. Report on a Case of Chromoblastomycosis, Puerto Rico J Pub Health & Trop Med **9** 169, 1933

2 Lane, C G. A Cutaneous Disease Caused by a New Fungus (*Phialophora Verrucosa*), J Cutan Dis **33** 840, 1915

3 Medlar, E M. A Cutaneous Infection Caused by a New Fungus, *Phialophora Verrucosa*, with a Study of the Fungus, J M Research **32** 507, 1915, A New Fungus, *Phialophora Verrucosa*, Pathogenic for Man, Mycologia **7** 200, 1915

4 Pedroso, A, and Gomes, J M. Sobre quatro casos de dermatite verrucosa produzida pela *Phialophora verrucosa*, Ann paulist de med e cir **11** 53, 1920

to one on the foot occurred on the right side of the neck, there has been no record of a lesion of this disease elsewhere on the body. We are therefore reporting here a primary lesion of dermatitis verrucosa or chromomycosis on the face of a man 67 years old.

HISTORY OF THE DISEASE

Historically, the infection in man was perhaps noted for the first time by Pedroso, in 1911 at São Paulo, Brazil. At that time the investigator named the disease the "black blastomycosis," because he had observed brown or black cells in histologic sections of diseased tissue. Clinically the condition in certain aspects resembled blastomycosis. This case was not reported until 1920, when with Gomes he published reports of 4 cases. The fungi found in each case were named *Phialophora verrucosa*. In 1915 Lane and also Medlar in the United States published the first case of chromomycosis in this country, in which the lesion occurred on the buttock of a 19 year old boy. The organism was studied by Thaxter and named *Phialophora verrucosa*.

In 1922 Terra, Torres, da Fonseca and de Area Leão⁵ studied a new case of dermatitis verrucosa, described the organism as *Acrotheca pedrosoi* and termed the disease "chromoblastomycosis" a blastomycosis produced by a colored fungus. Unfortunately, the name is still employed by many writers. Although the condition may simulate blastomycosis clinically, histologically it is not that disease, as has been pointed out by numerous investigators, especially by Wilson, Hulsey and Weidman⁶. The lesion may have the characters of several conditions or infections, such as tuberculosis, blastomycosis, coccidioidal granuloma, sporotrichosis, syphilis, a foreign body reaction and granuloma. There are seen in sections of diseased tissue, and occasionally in pus, brown thick-walled cells which may be unilocular or multilocular (fig 2). These cells do not in any sense of the word resemble true blastomycetes, for they do not show typical budding. The name chromoblastomycosis has nothing to do with the biologic nature of the organism, it refers only to the color of the microbe in tissue. Accordingly, the name was changed to chromomycosis by Moore and Almeida⁷.

During the years from 1920 to the present time numerous cases of chromomycosis have been reported, with various fungi as causative

5 Terra, F., Torres, M., da Fonseca, O., and de Area Leão, A. E. Novo tipo de dermatite verrucosa, mycose por *Acrotheca* com associação de leishmaniose, *Brasil-med* 2:365, 1922.

6 Wilson, S. J., Hulsey, S., and Weidman, F. D. Chromoblastomycosis in Texas, *Arch. Dermat. & Syph.* 27:107 (Jan) 1933.

7 Moore, M. and de Almeida, F. Etiologic Agents of Chromomycosis (Chromoblastomycosis of Terra, Torres, da Fonseca and Area Leão, 1922), of North and South America, *Rev. biol. e hyg.* 6:94, 1935.

agents Among the authors may be mentioned Mouchet and Van Nitsen,⁸ who found a case in Rhodesia, Cavalcanti,⁹ who in his thesis of 1924 at Rio de Janeiro described a case, Carini,¹⁰ who in the same year reported 2 cases from São Paulo, and in 1927 Montpellier and Catanei,¹¹ who reported the disease from Algeria Hoffman¹² in 1928 had a patient with this disease, and in the same year Bonne¹³ published a case from Sumatra In 1929 Borzone and Furno¹⁴ noted the condition in Argentina, and a few years later Balina, Bosq, Negroni and Quiroga¹⁵ described the first case from Buenos Aires Several other cases were reported from northern Brazil, and Nauck¹⁶ in 1931 described 2 more patients with chromomycosis from Rhodesia

In January 1933 appeared the second case of chromomycosis in the United States in which the disease was due to *P verrucosa* This report, published by Wilson, Hulsey and Weidman,⁶ is of interest chiefly because the infection occurred in a locality (Texas) widely separated from the region where the first case occurred (Boston) and secondly, because the lesion occurred on the foot In the following year appeared the publication of MacKinnon¹⁷ of the first case of chromomycosis in Uruguay, and in that case also the condition was due to *P verrucosa* This was the third case in which the disease was due to this organism and the

8 Mouchet, R, and Van Nitsen, R Sur une dermatite verruqueuse des noirs de la Rhodésie du Nord-Est, *Ann Soc belge de méd trop* 1 235, 1920-1921

9 de Mello Cavalcanti, J T Contribuição ao estudo das chromoblastomycoses, Thesis, Rio de Janeiro, 1924

10 Carini, A Sur la dermatite verruqueuse, *Bull Soc path exot* 17 227, 1924

11 Montpellier, J, and Catanei, A Mycose humaine due à un champignon du genre "Hormodendron *H algeriensis* nov sp," *Ann de dermat et syph* 8:627, 1927

12 Hoffman, W H La cromoblastomicosis en Cuba y la enfermedad de guiteras o "chappa," *Rev méd cubana* 39 420, 1928, Die Chromoblastomykose in Cuba, *Arch f Schiffs- u Tropen-Hyg* 32 485, 1928

13 Bonne, C Blastomycosis, with a Description of a Case of Chromoblastomycosis from Sumatra, *Geneesk tijdschr v Nederl-Indië* 68 705, 1928

14 Borzone, R A, and Furno, A Contribución al conocimiento de las blastomicosis americanas Primera observación de dermatitis verrucosa en la Argentina, in *Reunión de la Sociedad Argentina de Patología Regional del Norte* (1929), Buenos Aires, 1930, vol 1, pp 351-356

15 Balina, P S, Bosq, P, Negroni, P, and Quiroga, M Un caso de cromoblastomicosis, autoctono de Argentina, *Rev argent de dermatosif* 16 369, 1932

16 Nauck, E G La importancia de las investigaciones histopatológicas para el diagnóstico de la dermatitis verrugosa (cromoblastomicosis), *Rev méd german-iber-am* 4 671, 1931

17 MacKinnon, J E Estudio del primer caso uruguayo de cromoblastomicosis y "revista critica" sobre la enfermedad, *Arch urug de med, cir y especialid* 5 201, 1934

fourth in which the condition was caused by a *Phialophora*, since in 1 of the cases described by Pedroso and Gomes the condition was found to have been caused by *Phialophora macrospora*¹⁸

In 1933 a case of chromomycosis was reported by Carrión and Koppisch¹ in Puerto Rico, the first of several cases published by Carrión¹⁹ In the same year Martin, Baker and Conant²⁰ published from North Carolina the third case in the United States Recent communication with de Almeida, of São Paulo, Brazil, has disclosed a number of additional cases from that region

The case reported here is the fourth reported instance of this disease in the United States, the fourth in which the disease was due to *P. verrucosa* and the fifth in which it was due to a member of the genus *Phialophora* It would be safe to say that chromomycosis as a disease is fairly well distributed over several continents, particularly North and South America and the interlying islands, that it is caused by several organisms²¹ and that better clinical knowledge should reveal many more cases Recent communication with Dr F W Weidman, of Philadelphia, and with physicians in California has revealed additional cases

REPORT OF CASE²²

History—M S, a white man aged 67, of Creole-French descent, who was born in Missouri and had never been out of the state, presented himself in August 1938 at the Barnard Free Skin and Cancer Hospital, complaining of a lesion on the right cheek The family history was irrelevant The past medical history did not relate to his illness on admission He had had no operations At the age of 30 he suffered from stomach trouble due to lead fumes inhaled while working in a foundry He had had typhoid fever at the age of 40 and had had malaria several times There had never been symptoms referable to the cardiorespiratory system For the past four years he had suffered from rheumatism of the back and extremities There was no history of the ingestion of drugs

His illness on admission had its beginning ten years previously, when he had burned his right cheek with the sulfur of a match At that time he was engaged

18 Moore, M, and de Almeida, F P New Organisms of Chromomycosis, *Ann Missouri Botan Garden* **23** 543, 1936

19 Carrión, A L Chromoblastomycosis Preliminary Report on a New Clinical Type of the Disease Caused by *Hormodendrum Compactum*, Nov Sp, Puerto Rico J Pub Health & Trop Med **10**:543, 1935, Chromoblastomycosis A New Clinical Type Caused by *Hormodendrum Compactum*, *ibid* **11** 663, 1936

20 Martin, D S Baker, R D, and Conant, N F A Case of Verrucous Dermatitis Caused by *Hormodendrum Pedrosoi* (Chromoblastomycosis) in North Carolina, *Am J Trop Med* **16** 593, 1936

21 Moore, M The Organisms of Chromomycosis of North and South America, *Science* **83**:603, 1936, Chromomycosis, *Folia biol*, 1936, nos 61-65, pp 266-269 Wilson, Hulsey and Weidman⁶ Moore and de Almeida¹⁸

22 Case presented and discussed at the first annual meeting of the American Academy of Dermatology and Syphilology held Nov 14 and 15, 1939, at St Louis (*Arch Dermat & Syph* **40** 124 [July] 1939)

in loading and hauling wood and logs. The small burn healed slowly, and after healing a small spot appeared, which had gradually spread, over the ten year period, to the size noted when first seen.

Examination—On admission it was noted that the patient was of swarthy complexion, with large and pitted sebaceous follicular openings on the face. On the right cheek was an irregular discrete elevated pinkish lesion, with the medial border impinging on the nasolabial fold. The surface was covered with a thin dry adherent scale and did not bleed when the scale was removed. The epidermis under the scale was thin and intact, with no ulceration and with several bluish pits on the surface. The lesion measured 4 by 5 cm., was elevated about 0.5 cm., and firm and had a pearly appearance, with the border merging into the normal skin.

The general physical examination revealed a presenile man who moved with difficulty because of arthritis. The ocular and general reflexes were normal. The oral mucosa was normal, including the area lying directly under the lesion on the cheek. The teeth were dirty and carious. The lungs were normally resonant with no rales. The apex of the heart was in the sixth interspace and the anterior axillary line. The heart was regular, with no murmurs, and the blood pressure was 180 systolic and 120 diastolic. The liver was neither tender nor palpable, and the spleen was faintly palpable. The tone of the anal sphincter was fair. The prostate was moderately firm and enlarged. The extremities were normal, and there was no dependent edema.

Laboratory Examination—Urinalyses were normal. Results of blood sugar and sugar tolerance tests were within normal range. The nonprotein nitrogen content of the blood was 25 mg. per hundred cubic centimeters. Kahn reactions of the blood and spinal fluid were negative. On Sept. 10, 1938, the colloidal gold reaction of the spinal fluid was 4554444221. This may have been a laboratory error, as there were no symptoms or physical signs of any disease of the central nervous system. The albumin content and cell count of the fluid were normal, and a repetition of the colloidal gold test on another specimen six weeks later yielded a normal curve. Cultures of the spinal fluid gave negative results.

Röntgenograms of the skull were normal. The lungs showed normal pulmonary markings, but there were a moderate cardiac enlargement and diffuse dilatation of the aorta. The spine showed hipping and decided hypertrophic arthritic changes.

Histologic examination of the lesions revealed changes like those of granuloma with marked infiltration with various cells and giant cells of the Langhans type, within some of which the typical dark brown, thick-walled, multilocular cells could be seen. The epidermis was greatly thickened. A diagnosis of chromomycosis was made. Because of the lack of exudative material, a second biopsy was made for culturing. The organism *P. verrucosa* was identified in the culture.

Progress—To build up the iodide content, the patient was given mixed treatment, orally, for three weeks. The lesion regressed remarkably during this time, and his general condition and the arthritis so improved that he was able to walk without a cane. As he was to be presented to the clinic at the meeting of the American Academy of Dermatology and Syphilology in November 1938, he was given a placebo for the next six weeks. Since Nov. 15, 1938, he had been taking iodides by mouth, and the lesion was rapidly disappearing. The patient did not return for further investigation.

PATHOLOGY

Clinically the picture of chromomycosis may resemble one of several granulomatous lesions. In its early stages it may be confused with tuberculosis verrucosa cutis, epithelioma, blastomycosis, syphilis or

coccidioidal granuloma, in addition to various other granulomatous, mycotic infections. As the lesions progress in size, the hypertrophic changes appear definitely granulomatous, verruca-like, papular, nodular (some with pedicles) and psoriasiform and often showing ulceration and abscess formation. A crust may often be seen on the surface of the lesion, which offers no pain to the patient when it is removed, revealing a moist base, which on pressure may exude a mucoid, serous or purulent material within which may be found the brown, thick-walled, multi-locular fungous cells.

The sites usually selected by the fungus are the feet (the dorsum and sides) extending up to and above the knees and the hands, with the lesions occurring on the dorsal region, involving the fingers and wrist and extending to and somewhat above the elbows. The case reported by Lane and Medlar was an exception, as is the case reported here.

To date there has been little or no indication of pain or itching in the affected parts. There seems to be no lymphangitis or lymphangitic metastasis. The case of Carrión and Koppisch¹ seems to be an exception in that these authors stated the belief that a metastasis occurred to the forearm.

The microscopic changes observed in the tissue suggest one of the diseases previously mentioned, particularly tuberculosis. However, a number of points of difference can be distinguished in addition to the finding of the typical fungi, which at once suggest a diagnosis of chromomycosis. The epidermis shows a decided hyperkeratosis and acanthosis due to the hyperplastic changes in the epidermal cells, which result in the thickening, broadening and elongation of the interpapillary pegs. There can also be observed a certain grade of parakeratosis.

The corium, however, shows a decided change, with intense infiltration, edema and fibrosis. Discrete granulomatous lesions are observed, showing central areas of polymorphonuclear leukocytes in various stages of degeneration, numerous lymphocytes, plasma cells, eosinophils, Russell's fuchsin bodies, epithelioid cells, macrophages, fibroblastic changes, discrete microabscesses and giant cells of the Langhans or foreign body type arranged in tubercle-like fashion (fig. 1). Within these giant cells or in the abscesses the sclerotic cells of the fungus can easily be seen either as single cells or grouped in clusters. The picture is so similar to that of tuberculosis, as has also been pointed out by Wilson, Hulsey and Weidman, that except for the presence of *P. verrucosa* it is somewhat difficult to distinguish it from this disease.

DESCRIPTION OF THE ORGANISM

In tissue as has been pointed out before, the large sclerotic cells of the fungus are dark brown, thick-walled, spherical or irregular and

single or multiple, they reproduce by enlargement and cross wall formation, to form mulberry-like clusters, and never by budding. Occasionally one may be misled by a picture as seen in figure 2. In actively infected tissue these are the only forms noted. In old necrotic tissue there may be seen occasionally a germination of the cells to form short filaments, somewhat similar to those seen in figure 31, where the tissue has been inoculated on artificial mediums.

Since we were unable to express any fluid or exudate from the tissue, a biopsy specimen was taken, and the material was cut up into fine pieces aseptically and inoculated into fresh Sabouraud's maltose and Czapek's



Fig 1—Histologic section of chromomycosis. Note the tuberculoid reaction with giant cells. Hematoxylin and eosin stain ($\times 107$)

agar. Approximately six days after insemination small black colonies, the size of a pinhead, could be noticed on Czapek's medium. Several of the inoculated bits of tissue were then taken from the artificial medium, fixed in solution of formaldehyde, embedded in paraffin, sectioned and studied. The fungous cells developed, as seen in figure 3, first by an elongation of the cells and then by the sending out of irregular prolongations, which eventually became of somewhat uniform size, with cross wall production to form the type of mycelium seen on artificial substrates. Colonies developed on the Sabouraud maltose agar approximately eleven days after insemination. When the colonies grew to a suitable size, subcultures were made on various mediums in order to

study the morphologic picture produced, so that the genus and species might be determined

The development of the fungus on artificial mediums with the resulting morphologic changes have been considered by several writers. The essential features, however, may be repeated here for the sake of completeness. The strain of *P. verrucosa* isolated in the case described here is essentially similar microscopically to those found in the cases reported from Boston, Texas and Uruguay.

When first isolated on artificial substrates, the thick-walled brown cells seen in sections germinate to form multiseptate filaments, which

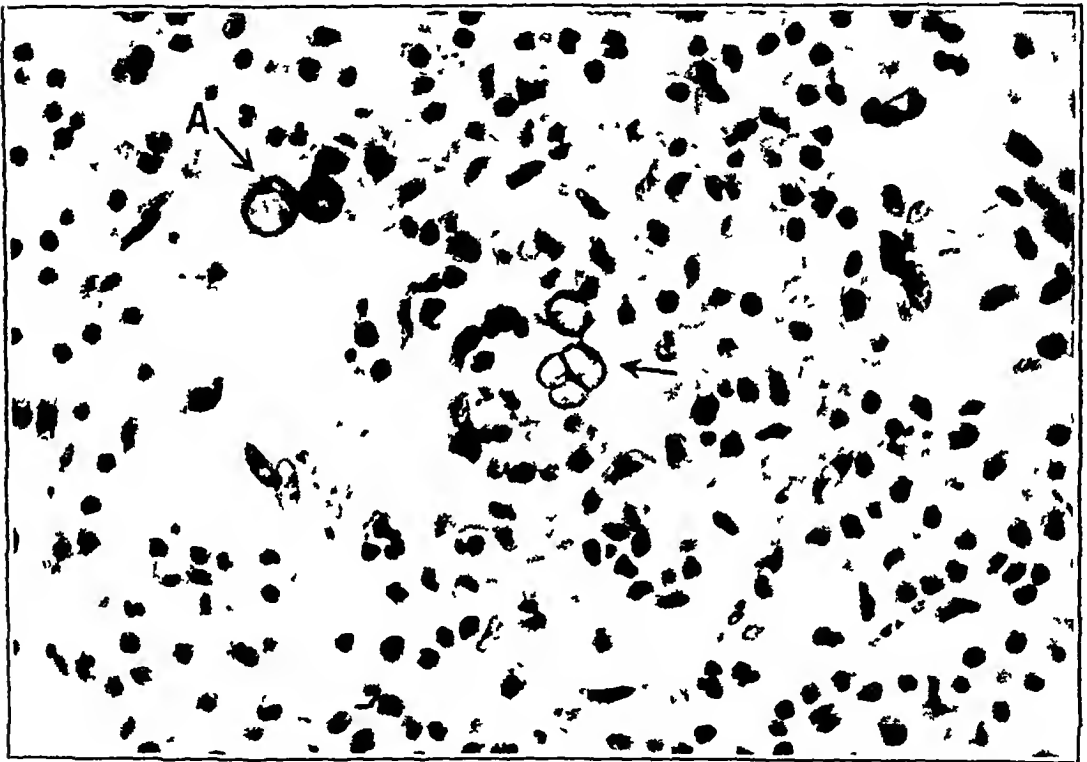


Fig 2—Tissue section. Note sclerotic, dark, thick-walled cells in giant cells. Hematoxylin and eosin stain ($\times 500$)

vary from approximately 2 to 5 microns in diameter. On some mediums, such as Czapek's or malt extract agar, these hyphae are of smaller diameter than on substrates having more peptone as a constituent. The hyphae, or filaments, are seen in culture either as isolated strands or in bundles (coremoid). This is particularly apparent in the compactly growing colonies.

On such mediums as peptone agar (fig 32) the filaments occur in the form of chains of cells or what is commonly referred to as a moniform growth. Among these cells there may also be seen larger, thick-walled forms, which seem to correspond to those seen in tissue. On Loeffler's agar these forms are more apparent and simulate more

closely the parasitic structures. The moniliform development, however makes up only part of the culture, since on a medium such as Sabouraud's dextrose or maltosé agar there are seen also the multiseptate



Fig 3—1, germinating sclerotic cells in tissue, hematoxylin and eosin stain ($\times 335$), 2, moniliform and chlamydosporic cells on peptone agar ($\times 335$), 3, early development of phialides on Sabouraud's maltose agar ($\times 335$), 4, phialides showing conidia held together by gloea on Czapek's agar ($\times 335$)

filaments seen in figure 33. The latter hyphae then serve as the progenitors of the phialides and conidia, or phialospores, which characterize *Phialophora*.

The phialides, or cup-bearing endogenous spore formers, vary somewhat on the different mediums, but they attain their greatest number and largest variety of forms on Czapek's medium (fig 34). These spore-bearing structures may be single or many celled, simple or branched, elongate or short, and terminal, lateral or alternate on a hypha. Just as the phialides may be of diverse forms so do the spores vary in shape and dimensions. They vary from small, spherical cells, approximately 2 microns in diameter, to ovoid or somewhat fusiform conidia, measuring approximately 1 to 3 by 2 to 4 microns. The conidia are usually seen as groups at the mouth of a phialide, held together more or less by a mucilaginous material termed gloea (fig 34). The conidia are then capable of germinating to form again the structures already mentioned.

Cultural Description—The strain of *P. verrucosa* isolated from the case reported here showed the following characteristics on various mediums.

Czapek's Agar (pH 4.3) (fig 45)—The fungus showed the most rapid growth on this medium, attaining a diameter of 4.3 cm after twenty-two days, with a penetration of the substratum. The colony was blue-black to ochraceous brown at the periphery. The central mycelium in the form of a button was aerial and rat gray. The filaments were 2 to 5 microns in diameter, brown, thick walled and multiseptate, showing moniliform development. The conidia were 1.5 to 2 by 2 to 4 microns, with many unicelled to multicelled, simple or branched phialides.

Sabouraud's Dextrose Agar (pH 5.6)—Growth was fairly rapid, the colony measuring 3.5 cm in diameter after twenty days showing little growth downward, with a sharply defined periphery. The color was slate gray to black for the aerial tufted mycelium, becoming olivaceous gray peripherally with some color diffusion into the agar. The filaments were 2 to 3 microns in diameter, light brown, and thin walled, with few cross walls. The conidia varied in size, measuring 1 to 3 by 1 to 4 microns, with many of them spherical, but mostly ovoid. The phialides were present in varying proportions and number.

Sabouraud's Maltose Agar (pH 5.6) (fig 47)—Growth was at the same rate as on the dextrose medium, attaining a diameter of approximately 3.7 cm after twenty days. The features were essentially similar to those on the dextrose medium.

Potato-Dextrose Agar (pH 5.9) (fig 46)—The colony was 3.3 cm in diameter after twenty days. The culture was dark olivaceous gray. The aerial growth was more or less felted with a central button, and was light olivaceous gray. The hyphae measured 3 to 4 microns in diameter, were dark brown and thick walled and showed many cross walls. The conidia measured 1.5 to 2 by 2 to 4 microns. The phialides were 4 to 5 by 7 to 11 microns. There were seen also a number of spherical thick-walled cells, 6 microns in diameter.

Yeast-Dextrose Agar (Difco Product pH 7.0) (fig 48)—The colony was 3.2 cm in diameter after twenty days' growth. The color of the moist periphery

was black with the aerial, centrally tufted mycelium dark gray. The filaments were 2 to 4 microns in diameter and multiseptate. The conidia measured 1 to 2 by 2 to 4 microns, and there were few phialides. Spherical thick-walled cells were 4 to 6 microns in diameter.

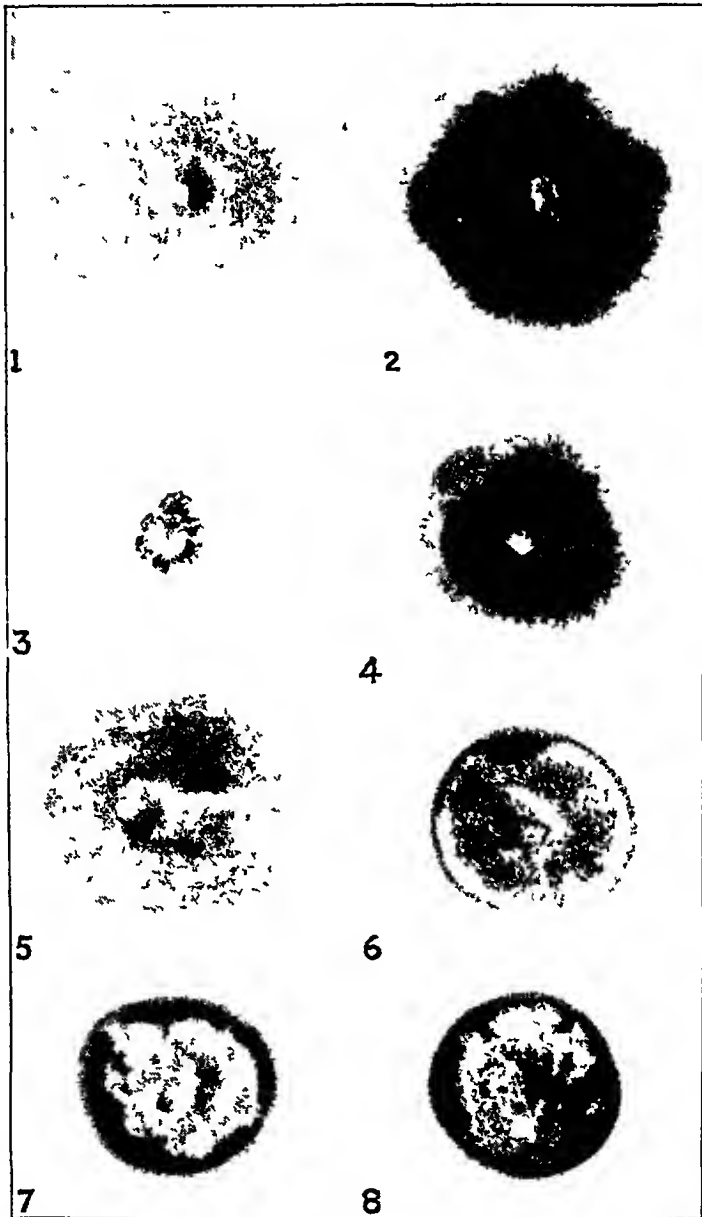


Fig 4—Cultures of *Phialophora*, four-fifths actual size. 1, *P. verrucosa* (Boston case) on Czapek's agar, 2, *P. macrospora* (São Paulo case) on Czapek's agar, 3, *P. verrucosa* (Texas case) on Czapek's agar, 4, *P. verrucosa* (Uruguay case) on Czapek's agar, 5, 6, 7 and 8, *P. verrucosa* (St. Louis case) on Czapek's agar, potato-dextrose agar, Sabouraud's maltose agar and yeast-dextrose agar, respectively.

Glycerin Agar (pH 7.0)—The glycerin agar cultures were highly distinctive in being decidedly raised above the surface of the medium and intense black, with the aerial hyphae showing a dark gray. The periphery was sharply defined and somewhat moist and shiny. The diameter of the colony was approximately 3 to 2 cm. after twenty days.

COMMENT

As a result of the relative infrequency of chromomycosis, it has not been possible for clinicians to determine the many clinical pictures that this disease exhibits. The finding of a lesion in an unusual location is therefore worthy of report. In spite of the fact that a large number of fungi may be involved as the incitants,²³ the macroscopic appearance of the lesion is essentially alike for all the microbes. The question of portal of entry or mode of infection was brought up by Wilson, Hulsey and Weidman. The disease is noted particularly in patients that have at one time or another been active in some type of rural work. The history usually shows that the lesion has developed after some trauma, no matter how slight. The chief sites have been the extremities. The lesion may be explained on the basis, therefore, that the organism is a saprophyte, growing on dead or decaying logs, as Conant²⁴ has attempted to show, and that the extremities are more subject to trauma and subsequent contact with the fungus in the natural habitat. This explanation serves possibly to elucidate the manner of infection in the patient described here, since he had traumatized his skin by burning and had been actively engaged in hauling and handling logs and lumber.

The confusing of chromomycosis with other mycotic infections, such as blastomycosis or coccidioidal granuloma, and with tuberculosis verrucosa cutis is not difficult to understand. Clinically there certainly is little at times, to differentiate one disease from the other. They are all granulomatous. Mycotic granulomas more or less affect the skin in the same manner. The histologic picture is essentially similar except perhaps for the intensity of reaction and the development of the lesion in certain patients dependent on the rapidity of reproduction and spread of the fungi in tissue. The organisms producing these diseases do not seem to liberate an exotoxin in the true sense of the word, but do their damage perhaps as actively proliferating foreign bodies. They are therefore not to be strictly compared with the typical granulomas produced by inanimate foreign substances, in which the foreign material remains localized, unless it is soluble in the skin and eventually becomes more or less walled off from the rest of the tissue.

²³ Wilson, Hulsey and Weidman; Moore and de Almeida;¹⁸ Martin, Baker and Conant.²⁰

²⁴ Conant, N. F. The Occurrence of a Human Pathogenic Fungus as a Saprophyte in Nature. *Mycologia* 29:597, 1937.

It is also curious to realize that of the 3 cases previously reported in which the condition was due to *Phialophora verrucosa*, in the first the lesion was on the buttock, in the second the foot was involved, and in the third there was an infection of the hand. In the fourth case reported here the face was involved.

A comparison of the several strains of *Phialophora* is interesting. The first culture isolated, that from Boston (fig 41), showed the greatest amount of growth. This possibly was because it had been growing on artificial mediums for the longest period. *P. macrospora*, isolated in Brazil (fig 42), showed similar cultural characteristics but differed in the size of conidia or spores. The strain of *P. verrucosa* isolated in Texas (fig 43) varied considerably macroscopically from all other strains in that it grew very slowly, attaining a diameter in twenty days which was approximately one-fifth that of the other cultures. The rate of development increased somewhat after this period, but the organism did not attain the magnitude of growth seen in the other strains. The organism from Uruguay (fig 44) and that from St. Louis (fig 45, 6, 7, 8) showed a similar rate of development but had some slight differences in gross appearance. It seems therefore, that in spite of the fact that all the strains of *P. verrucosa* from different localities were identical microscopically, they differed macroscopically and somewhat physiologically. This is in addition to the clinical observation that each affected a different part of the body.

SUMMARY AND CONCLUSIONS

The case of a 67 year old man with chromomycosis of the face for approximately ten years due to *Phialophora verrucosa* is presented. The location of the lesion was unusual, this being the first case, as far as we know, in which the face was a primary focus of infection following a trauma due to a burn with the sulfur of a match. It is also of interest that the patient acquired the infection in Missouri and had never been out of the state.

The lesion grossly simulated blastomycosis or tuberculosis verrucosa cutis. The diagnosis was made by finding the thick-walled, brown multilocular cells in the tissue and was subsequently confirmed by the isolation in culture of *P. verrucosa*. Although in culture the various strains of *P. verrucosa* from Boston, Texas, Uruguay and St. Louis are identical microscopically, they differ somewhat macroscopically. The Texas strain is decidedly slow in evolution.

P. verrucosa is described in culture, both macroscopically and microscopically. The granulomatous features of the histologic picture of this disease are discussed.

PERIPHLEBITIS NODULARIS NECROTISANS

AN ATTEMPT AT DEFINITION AND CLASSIFICATION

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One of the great faults of dermatologic nomenclature is the haste with which a new name is coined to designate anomalous symptoms of a previously well established clinical entity. To make matters even worse, the needless confusion which thereby ensues in the literature is kept up for years by the continued use of a name which in all common sense should have been relegated to limbo shortly after its conception. This holds particularly true of the term *periphlebitis nodularis necrotisans* which was first introduced by Philippson¹ in 1901. While the term has rarely appeared in the literature, it has done so frequently enough to warrant an analysis of the evidence pro and con to determine whether it is a clinical entity. I believe that I can offer sufficient evidence to prove conclusively that it has no claim as an original dermatosis, and that it is either an aberrant form of Bazin's disease or a tuberculid.

The symptoms of *periphlebitis nodularis necrotisans* are fairly constant, and my personal observation of this condition is probably confined to a dozen or more cases. In the large majority of these there were on the legs, and almost invariably in the usual location of Bazin's disease, a variable number of subcutaneous nodules, arranged in beadlike or linear formation. These nodules varied greatly in size, were sometimes painful on pressure and were usually pink to violaceous. At times there seemed to be no inflammatory changes in the overlying skin. As time went on the nodules became harder and darker and then shrank in size and eventually disappeared, leaving a brownish pigmented stain with some retraction or dimpling of the skin. Rather infrequently the nodules broke down and ulcerated and when they did they could not be distinguished clinically from Bazin's disease. More rarely the patient presented a series of twenty-five or more pea-sized violaceous nodules, which were painful and tender on palpation. Many of these nodules presented

Read at the Sixty-Second Annual Meeting of the American Dermatological Association Inc., Monte-Bello, Quebec, Canada June 2, 1939

1 Philippson, L. Ueber Phlebitis nodularis necrotisans (Beitrag zu dem Studium der Tuberculides von Darier) Arch f Dermat u Syph 55:215 1901

superficial erosions, and others ulcerated. In the latter eventuality, the lesions sometimes spread over the legs laterally and anteriorly as well as posteriorly. In a considerable number of the cases that I have observed the subcutaneous nodules of periphlebitis nodularis necrotisans appeared concomitantly with typical lesions of erythema induratum, and—what is of great importance—they disappeared under the orthodox treatment of Bazin's disease in exactly the same manner and time as the typical lesions of that well known entity. Again, when the two types of lesions were present, I have noted that small and new nodules have not progressed but have healed entirely at the same time that the larger typical lesions of erythema induratum resolved.

The differential diagnosis of periphlebitis nodularis necrotisans and periarteritis nodosa is not usually difficult. In the former disease the lesions are located on the legs only, with no constitutional symptoms, and the nodules and ulcers are not associated with other cutaneous changes. In periarteritis nodosa there are, besides the nodular lesions, occasional swelling and pain in the joints, elevation in temperature, cutaneous hemorrhagic spots, urticarial efflorescences and polymorphous erythema. Nodules occur on the arms as frequently as on the legs. Vascular involvement of the arms closely resembling livedo racemosa has been reported by Carol and Prakken.²

The histologic picture of periphlebitis nodularis necrotisans is interesting. The proponents of the theory that the condition is an entity from the histologic point of view have frequently cited Philipppson, yet a careful perusal of his paper shows that while he definitely stated that the most common histologic observations in his first case were partial or complete necrotization of the venous walls and their contents in the subcutis and a leukocytic infiltration within the vessel walls in the cutis, and that there seemed to be no interrelation microscopically with tuberculosis in that particular nodule, he did succeed in demonstrating the tubercle bacillus in two other nodules and in producing tuberculosis by inoculating the eye of a rabbit with a fragment of one of them. This to my mind proves that the eruption in Philipppson's case was definitely tuberculous. Even Philipppson himself was convinced that the appearance of the lesions in his case resembled the description of tuberculids by Darré in 1896, and he so stated in the opening paragraph of his paper. There is no doubt that the histologic picture of destruction of the veins by necrotic degeneration of their walls with no evidence of tuberculosis occurs in a number of specimens while an equal, if not a greater, number show tubercles and the other characteristic changes of tuberculosis. Why does this discrepancy occur? I believe that it can be

² Carol, W. L. L., and Prakken, J. R. Die kutane Form der Periarteritis nodosa, *Acta dermat-venereol* 18: 102 (Feb) 1937.

best explained in the words of the late Walter Highman³ before the Section of Dermatology and Syphilology of the New York Academy of Medicine, on March 4, 1930

Because [the histologic picture of erythema induratum did not appear] in the lesion examined in this patient does not prove that it would not be found in another lesion I think in this discussion we have the pseudophilosophy Molière referred to in his play "Les précieuses ridicules"

If you take one lesion from a patient with erythema induratum, Bazin, you might find the structure of tuberculosis and of an ordinary inflammation in the same specimen, indeed in the same section That is so typical of all tuberculosis In cases that are clinically erythema induratum, Bazin, you may find tuberculous structures in some and not in others

To my mind, Highman was right in his statement, it might well be that the apparent discrepancies in histologic work would greatly diminish if two, three or even more different biopsy specimens were taken in the same case instead of a large number of serial sections from a single piece of tissue I have not infrequently observed a complete reversal of a histologic report after the examination of a second or even a third specimen

Let me now consider the opinions of various American dermatologists as to the entity of this condition A case of periphlebitis nodularis necrotisans was presented by Eller⁴ before the New York Dermatological Society on May 15, 1928 The patient, a woman aged 24, stated that the eruption had been present for two years On the lower extremities there were many reddish elevations, some showing a tendency to linear formation There was no histologic report Drs G M MacKee and H H Whitehouse made a diagnosis of Bazin's disease Dr Highman said

Why call it periphlebitis nodularis necroticans? Bazin's disease is a perivascular infiltration, and for a good reason The infiltration cannot escape blood vessels In fact, a characteristic feature of Bazin's disease is the relation of the infiltration to blood vessels A name like this is another example of complicating dermatology in the most fatuous manner possible It is unjustifiable by fact or necessity

A case of periphlebitis nodularis necrotisans was presented by MacKee⁵ before the New York Dermatological Society on Jan 28, 1930 The patient was a man aged 20 The eruption consisted of deep-seated hard and slightly painful nodules Most of them ulcerated, and the ulcers lasted for many months before healing The eruption was of

³ Highman, W, in discussion on Eller, J J Periphlebitis Nodularis Necroticans, Arch Dermat & Syph 22:722 (Oct) 1930

⁴ Eller, J J Periphlebitis Nodularis Necroticans, Arch Dermat & Syph 19:138 (Jan) 1929

⁵ MacKee, G M Periphlebitis Nodularis Necrotisans, Arch Dermat & Syph 22:367 (Aug) 1930

two years' duration Under the microscope there was a dense infiltration of round cells in the lower part of the cutis, but mostly in the fat and around thickened blood vessels Giant and epithelioid cells were absent There were a few plasma cells The case was presented as one of periphlebitis nodularis necrotisans with the understanding that this condition was an aberrant form of Bazin's disease In the discussion Drs Wise, J F Fraser, E R Maloney and Highman made a diagnosis of Bazin's disease The same patient was shown by Wise⁶ before the Manhattan Dermatological Society, on Feb 11, 1930 A patient was presented by me⁷ before the New York Academy of Medicine, Section of Dermatology and Syphilis, on Nov 8, 1933, with the diagnosis of periphlebitis nodularis necrotisans The patient was a man aged 40 He presented a number of indolent violaceous red nodular lesions on the legs, some of which had necrosed and broken down to form shallow ulcers They had been present for four months The histologic report was of a nondescript picture Roentgenograms of the chest showed an infiltrated shadow in the apex of the left lung The shadow was fairly sharp and was typical of tuberculosis In the discussion Dr M B Sulzberger stated

It would be best to drop such terms as 'periphlebitis nodularis necroticans' and "dermatitis necrotica" in the designation of ulcerative processes on the lower legs such as that in Dr Bechet's case Philippson, who applied the latter term to two similar cases, later read Darier's description of papulonecrotic tuberculids He then recognized the resemblance between Darier's tuberculids and the condition in his cases and fortunately had the opportunity to reexamine the patients After a long and tedious investigation he was able to prove histologically and by animal inoculation that the condition in both of his cases was tuberculous For this reason, it is now generally accepted that these terms, as well as "hydroadenitis suppurativa," which Pollitzer was the first to use for a picture clinically somewhat similar, are merely old names used before the tuberculous etiology of this entity was recognized In the vast majority of cases of this nature the lesions can be proved to be tuberculids provided one takes sufficient time and pains and has the opportunity to study a sufficient number of lesions histologically by the injection of tuberculin, and by guinea-pig inoculation

Dr Sigmund Pollitzer said

Dr Sulzberger has already referred to Philippson's work The cases that he described were identical, and histologic examination showed the same picture that I had found a year or two earlier and reported under the name of "hydroadenitis suppurativa" Philippson and I corresponded later on the subject and agreed on the essential features Five or six years later Darier established the group of the tuberculids Both Philippson's term and mine have been eliminated by the increase in knowledge, and I see no reason for reviving them

6 Wise, F Periphlebitis Nodularis Necrotisans, Arch Dermat & Syph
22 546 (Sept) 1930

7 Bechet, P E Periphlebitis Nodularis Necroticans, Arch Dermat & Syph
29 753 (May) 1934

SUMMARY

Clinical, and to a certain extent, laboratory, evidence indicates that periphlebitis nodularis necrotisans is not a clinical entity but an aberrant form of Bazin's disease or, less likely, a member of the large group of papulonecrotic tuberculids. This has been proved, first, by the testimony of Philipsson, the originator of the name, who besides admitting the similarity of the syndrome to tuberculosis of the skin, succeeded in finding the tubercle bacillus in the nodules and in producing tuberculosis by inoculating a rabbit with a fragment of one of them, second, by the frequency with which I have observed the concomitant appearance of the subcutaneous nodules of so-called periphlebitis nodularis necroticans and of the typical lesions of erythema induratum, and the simultaneous healing of both types of lesions under the usual therapy of erythema induratum, third, by the almost unanimous opinion of American dermatologists that periphlebitis nodularis necrotisans is an aberrant form of erythema induratum of Bazin and not a clinical entity, and fourth, by the testimony of such excellent histologists as the late Drs Pollitzer and Highman to the effect that despite the conflicting histologic reports the term periphlebitis nodularis necrotisans should be dropped and the syndrome hitherto described under that name classed as a tuberculoid or tuberculous dermatologic manifestation.

In conclusion, I hope that my effort to prove the nonexistence of a dermatosis with another long name may be successful, thereby simplifying to a slight degree the still formidable and occasionally unjustifiable nomenclature.

ABSTRACT OF DISCUSSION

DR HAROLD N. COLE, Cleveland. Perhaps a little more difficulty is encountered in the treatment of erythema induratum in Cleveland than in New York, but I should like to know what new type of treatment it is that gives such uniform and good results.

DR MARION B. SZLZBERGER, New York. Dermatologists must agree today with Brocq's idea of *reaction cutanée* in regard to many of the morphologic entities. For example, in nodose erythemas, in multiform erythemas, in sarcoid reactions and in similar conditions it has been proved that closely similar or almost identical clinical and microscopic pictures can be produced by different etiologic agents. It would be tempting to say that the same remark may apply to those conditions of the legs diagnosed as erythema induratum or papulonecrotic tuberculid and that they too may have a different cause in different cases. Unfortunately, this has never been proved to be true. It does not seem that any typical case has ever been proved due to any etiologic agent other than the tubercle bacillus. Thus a case of nodose erythema may be caused by a streptococcus, by the lepra bacillus, by the virus of lymphogranuloma venereum, by a drug such as bromide or iodide or salicylate and by any one of many other etiologic agents. However, there are no authenticated and well studied cases of Bazin's disease with the typical clinical picture and histologic changes and no case of typical papulonecrotic tuberculid in which causation by an agent other than the tubercle

bacillus has been proved. All typical cases in which extensive, thorough and proper examinations have been made have been shown to be of undiscoverable cause or have eventually been shown to be of tuberculous origin. In these etiologic examinations, the determination of macroscopic or microscopic changes must necessarily play a minor role. For since one starts by granting the premise that identical or similar cutaneous changes may be the result of different causes, one can obviously draw no binding conclusion as to causation by means of mere morphologic analysis. In determining the cause of these cutaneous pictures, one must go beyond morphologic factors and consider epidemiologic ones, immunologic reactions and particularly bacteriologic investigations. Proper bacteriologic investigation of a cutaneous lesion suspected of being a tuberculid may have to consist of many biopsies of abundant tissue from various lesions in different stages of development and involution and numerous animal inoculations with this material. It is sometimes necessary to inoculate as many as ten guinea pigs from each specimen of tissue, and all the animals should be allowed to live until one is certain that tuberculosis will not develop in some one of them. Wherever one has been fortunate enough to have facilities for such studies, it has eventually been shown that in typical cases of Bazin's disease and papulonecrotic tuberculids tubercle bacilli are usually present, regardless of whether the histologic morphe presents banal perivascularitis or tubercle structures. In this manner, the lesions in Phillipson's own cases of "periphlebitis nodularis necroticans" were shown to be tuberculids, and Phillipson himself published this fact and withdrew his descriptive term in favor of Darier's etiologic designation.

DR PAUL E. BECHET, New York. In response to Dr. Cole's question as to what constitutes the orthodox treatment of erythema induratum, I beg to state that I consider aurotherapy, roentgen irradiation, the injection of tuberculin and a high vitamin intake as the routine or orthodox treatment. Of all these remedies I have found that the use of gold compounds and roentgen irradiation have given me the best results, and I may be drawing a withering fire on myself by stating that I have even observed several cures by means of their use. At the same time, I do not wish to convey the idea that I believe these remedies are specific, as they not infrequently dismally fail. I am sorry that Dr. Cole misconstrued the definition of the word "orthodox," which means "in accordance with sound doctrine." Such a definition certainly does not convey the idea of infallibility. I feel sure that erythema induratum is just as successfully or as unsuccessfully treated in Cleveland as in New York, and I hope that Dr. Cole's delusions about the superiority of New York therapy will not become chronic.

BULLOUS ERUPTION FOLLOWING SULF-ANILAMIDE THERAPY

ERVIN EPSTEIN, MD

OAKLAND, CALIF

The expansion of the therapeutic application of sulfanilamide has been more or less paralleled by the recognition of apparently new toxic reactions to the drug Loveman and Simon¹ recently reported a case of bullous stomatitis in which a single bullous lesion developed on the hand as a result of sulfanilamide therapy Because of the limitation of the eruption, pemphigus was not suggested clinically, although it obviously might have been so considered had similar lesions occurred over a more widespread area of the body Small vesicular lesions have been noted in sulfanilamide eruptions by Menville and Archinard² and by Tedder³

Since the introduction of sulfanilamide as an agent in the treatment of pemphigus by Caro,⁴ conflicting opinions regarding its worth have been expressed⁵ It is interesting that sulfanilamide may lead to the development of tense bullae on apparently normal skin, in association with definite constitutional symptoms

REPORT OF A CASE

O N, a 54 year old white man, fell on July 5, 1939, bruising and lacerating his left hand On the following day his hand began to swell, and there were marked pain and tenderness He entered the hospital on July 7, and a diagnosis of acute cellulitis of the left hand with palmar space infection was made Sulfanilamide was administered orally, and he made a prompt recovery, being discharged on July 13 During his stay in the hospital he received 20 grams (13 Gm) of the drug four times a day, administered with an equal amount of sodium bicarbonate A total of 400 grams (26 Gm) of sulfanilamide was ingested

1 Loveman, A B, and Simon, F A Fixed Eruption and Stomatitis Due to Sulfanilamide, Arch Dermat & Syph 40:29 (July) 1939

2 Menville, J G, and Archinard, J J Skin Eruptions in Patients Receiving Sulfanilamide, J A M A 109:1009 (Sept 25) 1937

3 Tedder, I W Toxic Manifestations in the Skin Following Sulfanilamide Therapy, Arch Dermat & Syph 39:217 (Feb) 1939

4 Caro M R Pemphigus Treatment with Sulfanilamide Arch Dermat & Syph 37:196 (Feb) 1938

5 See for example Feldman, S Pemphigus Treated with Sulfanilamide Sulfanilamide Eruption, Arch Dermat & Syph 39:601 (April) 1939 and the discussion following

When he left the hospital, the patient felt perfectly well. However, he was of necessity exposed to the sunshine that afternoon, although the exposure was not excessive. The next day decided edema developed on the face and hands. The skin over the shoulders became reddened, and a patchy erythematous pruritic eruption rapidly spread over his chest and back until his entire body was covered with cutaneous lesions.

I first observed the patient on July 14. At this time he presented a generalized coalescing morbilliform eruption. His face was edematous. Both hands were diffusely swollen to about twice their normal size. He complained of feeling weak, tired and feverish. His temperature, taken orally, was not elevated. The following day large tense bullae appeared on the dorsum of his right hand and on his right forearm. The surrounding skin was not involved except for the underlying edema. During the following two days about twelve such bullous lesions appeared. On the forearm they coalesced to form a multilocular plaque.

He made a prompt recovery with local therapy and was completely free of lesions on July 21.

COMMENT

It is not claimed that the bullous eruption in this patient could have been confused with that of pemphigus on the basis of the distribution of the lesions or of the course of the eruption. However, the individual bullae on the right hand and forearm were clinically indistinguishable from those seen in pemphigus. Therefore, in treating this disease with sulfanilamide one must realize that apparent clinical progression may be due to a toxic reaction to the drug rather than to the disease itself. Each case must be evaluated in the light of the knowledge that sulfanilamide may cause bullous lesions. Holland⁶ noted that the pemphigus in his patient became aggravated when large doses of sulfanilamide were administered.

That this patient was photosensitive is indicated by the initial appearance of the eruption on the exposed portions of the body, i. e. the face and the dorsa of the hands as well as by its maximum intensity in these areas. The fact that the reaction did not start until after exposure to sunlight further confirms this.

Perhaps the solar sensitivity constituted the basic etiologic agent in the production of the bullae. This would be analogous to the blister formation occasionally encountered in pellagra and severe sunburn. However, this patient said that he had not had more than minimum exposure to the sun, and there was no erythema present to lend clinical confirmatory evidence of sunburn.

SUMMARY

A report is presented on a patient in whom a bullous eruption developed after the administration of sulfanilamide.

⁶ Holland, M., in discussion on Feldman.⁵

It is suggested that the employment of sulfanilamide in the treatment of pemphigus may lead to confusion, as the medication may cause lesions similar to those seen in the disease being treated

NOTE—While this paper was in press, two additional examples of bullous eruptions following sulfanilamide therapy have been reported Bettley and Simon⁷ described a similar case. A patient with a severe bullous eruption following the ingestion of sulfapyridine was exhibited by Omens and Robbins⁸ before the Chicago Dermatological Society on March 15, 1939

1624 Franklin Street

7 Bettley, F. R., and Simon, P. A Bullous Eruption Due to Sulphanilamide, *Brit. M. J.* **1**:1177 (June 10) 1939

8 Omens, D. V., and Robbins, J. B. Severe Toxic Bullous Eruption Following the Use of Sulfapyridine, *Arch. Dermat. & Syph.* **40**:633 (Oct.) 1939

DANGERS IN THE USE OF COSMETICS

GEORGE L. WOLCOTT, M.D.

ASBURY PARK, N. J.

Cole¹ has stated

There seems to be an alarming increase in the use of cosmetics—and along with this a coincident increase in the dangers due to their use. The esthetics of cosmetics are the concern of the physician only secondarily, but we should do everything in our power to call to the attention of the public the damage resulting from their use.

To the average person, whether physician or layman, cosmetics represent a highly commercialized development of the current century, their composition and the dangers attendant on their use are known to but a few select groups. Lerner² reported that cosmetics have been used by women from the time of the earliest records and quoted numerous recipes for beauty which were in vogue perhaps more than twenty thousand years ago. Oddly enough, a study of various historical references³ to the nature of cosmetics reveals that the so-called "modern cosmetics" can be traced back many centuries.

Lain⁴ stated

Cosmetics did not present a serious pathologic problem until after the beginning of the twentieth century. Cases of cosmetic dermatoses became so frequent between the years 1910 to 1925 that public health agencies began an organized attack.

Wilbert,⁵ of the United States Public Health Service, in 1915 presented a collection of various reports of injuries from cosmetics.

There have been sporadic organized attempts against the use of dangerous cosmetics, but most of the available references have dealt with small groups or even single cases of injuries from cosmetics. The

The material in this paper represents work done for the Department of Public Health while the author was a student at the College of Physicians and Surgeons, Columbia University. The review is based on articles published before the establishment of the Food, Drug and Cosmetic Act of 1938, and the descriptions cited do not necessarily represent the composition of the respective cosmetics at the present time.

1 Cole, H. N. The Dermatoses Due to Cosmetics, *J. A. M. A.* **82** 1909-1911 (June 14) 1924.

2 Lerner, C. History of Feminine Beautification, *Arch. Dermat. & Syph.* **26** 1022-1031 (Dec.) 1932.

3 (a) Downing, J. G. Cosmetics—Past and Present, *J. A. M. A.* **102** 2088-2091 (June 23) 1934. (b) Levin, O. L. Cosmetics—Use, Historical and Modern, *M. Rec.* **139** 292-294, 1934. (c) Lerner².

4 Lain, E. S. Cosmetic Eruptions, *South. M. J.* **25** 718-722, 1932.

5 Wilbert, M. I. Cosmetics as Drugs, *Pub. Health Rep.* **30** 3059-3066, 1915.

purposes of the present paper are to present an organized review of selected literature on cosmetics, to indicate briefly the composition of important cosmetics, to report proved cases of damage from their use and to indicate to what extent the consumer is protected by law, by the medical profession and by other agencies. For the reports cited I make no claim to completeness, with respect either to the nature of the cosmetics or to their dangers.

INCIDENCE OF INJURIES FROM COSMETICS

Tobias,⁶ in 1932, declared that the list of dermatoses due to external irritants is so large that one is impressed with the importance of having a list of irritants available for reference. In 1933 Hollander⁷ reported that dermatitis produced by cosmetics through direct contact was becoming a more frequently established and recognized condition but that the specific agent responsible had to be ferreted out of an almost endless number of so-called beauty preparations. One year later Downing⁸ added his observations that with such a great increase in the cosmetic business there has been an alarming increase in the number of local disturbances of the skin and that some systemic results have been reported, every busy dermatologist observes one or more cases a week of some condition resulting from cosmetics, but few report these cases.

Goodman,⁸ an outstanding authority in cosmetic dermatology, reported in 1930 that the number of persons who are sensitive to the ingredients of ordinary cosmetics is small, on the whole, throughout the country, it would be difficult to collect at any one time 100 persons who have been harmed by the application of cosmetics. Goodman, however, admitted that in many cases cosmetic injury is unrecognized by the ordinary practitioner.

In 1927 Cole⁹ reported the results of an investigation conducted by the American Medical Association, comprising 62 returns from a questionnaire sent to 437 dermatologists throughout the United States and 23 reports from another source. There were 111 reported cases of injury from hair dye (of which only 74 were reported by dermatologists). Of 137 reports of injury from various cosmetic nostrums, only 43 were reported by dermatologists. Forty-three additional cases of injury from hair tonic were reported, and injuries from the use of twenty-three miscellaneous preparations were listed. There was no indication of the period during which these injuries occurred.

6 Tobias, N. Cosmetics, *J. Missouri M. A.* 29:63-69, 1932.

7 Hollander, L. Dermatitis Produced by Cosmetics, *J. A. M. A.* 101:259-261 (Jul. 22) 1933.

8 Goodman, H. Cosmetics and Your Skin, *Hygeia* 8:123-125 (Feb.) 1930.

9 Cole, H. N. Investigation of Injuries from Hair Dyes, Dyed Furs and Cosmetics *J. A. M. A.* 88:397-399 (Feb. 5) 1927.

At the Lam-Roland clinic (Oklahoma City) in 1930, there were 285 cases of dermatitis of various types, in 42, or 11 per cent, of such cases, the eruption occurred over the face, a diagnosis of cosmetic dermatitis was made in 32, or 75 per cent, of the series of facial eruptions, this represented about 11 per cent of all cases of dermatitis observed during the year ¹

It is thus evident, although adequate statistics are lacking, that the incidence of injury from cosmetics is extremely small especially so when one considers the extent of the cosmetic industry and the tremendous number of persons using these preparations several times each day. Nevertheless, a problem does exist and the physician and the public health officer should be aware of the fundamental principles involved.

The earlier and more severe cosmetic injuries were to a great extent systemic poisonings from dangerous substances, such as lead and mercury. The cosmetic manufacturers today, cognizant of these earlier, more or less tragic experiments, have rid their industry of substances causing severe systemic reactions, in fact, in fairness to the industry, it should be reported that many of the larger and more reputable firms maintain laboratories for the purpose of eliminating harmful ingredients.

At present, the injuries from cosmetics seem to have been reduced to dermatologic, and more particularly allergic, manifestations. The cosmetic racketeer of today is that one who uses ingredients in his products that simply make a better physical and esthetic preparation, regardless of their nature or their potential dangers, and many racketeering companies exist and flourish at present.

Germany seems to have made considerable progress in regulation of the cosmetic industries. With respect to statistics, Krantz ¹⁰ reported that, of some 2 500,000 Germans that regularly dye their hair, 20 of 30,000 are slightly affected by the dye and 400 of 500,000 severely so. 'Most of the metallic dyes are forbidden in Germany.' The use of lead in cosmetics in Germany has been forbidden for at least forty years according to Carleton ¹¹.

TOILET POWDERS—COMPOSITION AND DANGERS

Carleton ¹¹ stated

Toilet powders consist of a mixture of animal or vegetable powders, colouring matter, and perfume. The vegetable powders include rice, wheat, corn flour, starch, acacia, and tragacanth. The mineral powders in use are chalk, talc, kaolin, magnesium carbonate, bismuth nitrate or carbonate, and zinc oxide. The dyes may be of vegetable origin or may be aniline derivatives. Various ethereal oils are used as perfumes, and orris root is frequently employed as a fixative.

10 Krantz, W. Injuries to the Skin Caused by Cosmetics, *Med Klin* **32** 209-212 1936

11 Carleton, A. Cosmetics Uses and Dangers, *Brit M J* **1** 999-1001, 1933

In addition, some widely advertised powders contain impurities and metals such as lead, bismuth, arsenic and mercury ¹⁰ The most dangerous powder ingredient which apparently is scarcely used at present in any part of the cosmetic industry, is lead, lead carbonate and lead acetate produce excellent powders from the physical and esthetic aspect

That vegetable powders injure the skin through swelling of the granules of powder in the cutaneous fat and that mineral powders irritate because of sharp edges and spicules of grains of some powders, especially those containing calcium sulfuricum and terra silicea was stated by Kapp ¹²

As early as 1881 there were reports of systemic poisoning from a cosmetic containing lead carbonate, Holland ¹³ reported the cases of 2 sisters in whom poisoning was demonstrable by bilateral wrist drop and spasms In Barron and Haben's ¹⁴ famous report of 1921 were described 5 cases (in 4 of which the damage was fatal) of lead poisoning in the women of a single family, resultant from the steady use of a powder, "flake-white," composed of pure lead carbonate

Tuttle ¹⁵ observed 5 cases of poisoning in 1884 from a cosmetic powder containing an insoluble preparation of bismuth

It is interesting to note the increase in the apparently allergic reactions to certain ingredients of face powders, notably orris Freudenthal ¹⁶ reported several cases of allergic disturbance of the upper part of the respiratory tract, in one of which the condition was proved to be due to orris in face powder

The results of a study by Balyeat ¹⁷ of 1,000 cases of hay fever and asthma are extremely interesting from the point of view of the dangers of using face powders containing orris Of 180 cases of hay fever and asthma in patients under 14 years of age, in 18 or 10 per cent, there was a reaction to orris Of 82 cases of perennial hay fever in adults, in 39, or 47.5 per cent there was a definite reaction to orris Of 365 cases of asthma studied, orris was the sole cause in only 1, a chief factor in 26, or 7.1 per cent, and a contributing factor in 48, or 10.4 per cent Of 373 cases of seasonal hay fever, there was a reaction to orris in 27, or 7.2 per cent, in spite of the etiologic importance of pollen

¹² Kapp, cited by Downing ^{3a}

¹³ Holland I W Chronic Lead Poisoning from Lead Cosmetics, Rep Bd Health Kentucky (1880) 3 111-121 1881

¹⁴ Barron M, and Haben, H C Lead Poisoning with Special Reference to Poisoning from Lead Cosmetics Am J M Sc 162:833-862 1921

¹⁵ Tuttle, cited by Cole ¹

¹⁶ Freudenthal W Tobacco Alcohol and Cosmetics in Relation to Upper Respiratory Tract Laryngoscope 37:217-230 1927

¹⁷ Balyeat R M The Importance of Orris Root as an Etiologic Factor in Hay Fever and Asthma, J Lab & Clin Med 13:516-522, 1928

in seasonal disease Cooke,¹⁸ Phillips¹⁹ and Rackeman²⁰ reported similar results of determinations of hypersensitivity to orris among patients with hay fever and asthma, although their figures were somewhat lower

Robinson²¹ in 1915 reported 2 cases of lead intoxication, in each of which there were wrist drop, muscular atrophy, a lead line on the gums and paralysis from a lead carbonate face powder

FACIAL CREAMS—COMPOSITION AND DANGERS

Cold creams, according to Downing,²² are prepared from a vegetable or mineral oil, such as oil of almond, yellow wax or liquid petrolatum, to which is added a small amount of sodium borate to aid emulsification. Among other substances which may or may not be present in cold creams are palmitates, stearates and fatty alcohols, lead and mercury are rarely used in these preparations at present. Most of the substances used are relatively innocuous.

Cleansing creams, in spite of the allegation that they replace soap and water, are nothing more than mixtures of liquid petrolatum and higher melting point greases, fats and waxes.

MacKenna's²² report, written in 1930, indicated that he was almost radically convinced of the dangers of facial creams, he suggested that the paraffin in many cold creams may lead to an increase in the number of cases of rodent ulcer and of epithelioma of the face in women, furthermore, he expressed a belief that the physical action of both cold and vanishing cream leads eventually to the production of acne rosacea. Because of the lack of supportive evidence, one is not inclined to consider MacKenna's fears seriously.

Two experimental investigations of facial creams were apparently inspired by MacKenna's statements. Downing²² cited one series in which not a single case of dermatitis occurred from the use of vanishing or cold cream of a special formula in a group of 25 subjects. In another group¹¹ vanishing cream was used on 40 subjects and proved harmless to 24 (although 3 had naturally dry skins), it proved beneficial in 13 cases, and in only 1 did it cause dryness.

The questionnaire of the American Medical Association, as reported by Cole,⁹ showed that of the 137 reports of injury from various cosmetics, 9 were from cold creams, 4 from bleaches, 5 from powders and

18 Cooke, cited by Balyeat¹⁷

19 Phillips, cited by Balyeat¹⁷

20 Rackeman, cited by Balyeat¹⁷

21 Robinson, cited by Cole¹

22 MacKenna, R M B. Modern Cosmetic Preparations. Chemical Composition and Pathological Developments Attributable to Them, *Brit M J* 1 899-902, 1930

8 from rouge and the like, mercury bichloride and ammoniated mercury were found to be the commonest offending ingredients

Woltman²³ described in 1922 a case of severe systemic lead poisoning in a woman who had used a face cream with a high lead content. As recently as 1936,²⁴ a case of chronic lead poisoning from a grease paint, of high lead content, was reported. Apparently, then, the manufacturers have failed to profit by the earlier tragic lessons of lead in cosmetics, or they simply choose to ignore the dangers.

Two cases of dermatitis of the eyelids from facial cream, in 1 of which camphor was the offending ingredient and in the other perfume (methylheptene carbonate), were reported by Rattner.²⁵ In another case²⁶ atopic dermatitis and angioneurotic edema of the face were reported as due to methylheptene carbonate, the perfume in a facial preparation. These cases occurred rather recently.

In 1937 a dermatologist queried the Bureau of Investigation of the American Medical Association as to the ingredients of Jergen's lotion, as he had a patient with a severe dermatitis from its use (patch test positive). Because of the failure of the manufacturer to cooperate, it was impossible to trace the offending ingredient.²⁷

LIPSTICKS—COMPOSITION AND DANGERS

Sulzberger and Goodman²⁸ said

The lipstick in common use has a fatty base, commonly containing several of the following ingredients: yellow wax, paraffin, petrolatum, hydrous wool fat, castor oil, stearic acid and cetyl alcohol. In this base are incorporated perfumes, dyes and lakes.

According to Baer,²⁹ a dibrom or tetrabrom derivative of fluorescein is used to set the color and make it permanent, the dyes used in the manufacture of lipstick are of vegetable and aniline origin.

Sulzberger and Goodman²⁸ reported a series of recent cases, 12 of cheilitis and 2 of dermatitis of the face (without cheilitis), due to lipstick, 8 of the patients were hypersensitive to the indelible dyes.

²³ Woltman, H. W. Lead Poisoning from Face Enamel, *J. A. M. A.* **79** 1685 (Nov. 11) 1922.

²⁴ Bartleman, E. L., and Dukes, C. Chronic Lead-Poisoning Due to Theatrical Grease Paint, *Brit. M. J.* **1** 528-530, 1936.

²⁵ Rattner, H. Dermatitis of Eyelids, *J. A. M. A.* **103** 180-181 (July 21) 1934.

²⁶ Hoffman, M. J., and Peters, J. Dermatitis Due to Facial Cream, Caused by Methyl Heptene Carbonate, *J. A. M. A.* **104** 1072 (March 30) 1935.

²⁷ Jergen's Lotion. A Lesson in the Art of Correspondence, report of the Bureau of Investigation, *J. A. M. A.* **108** 135-136 (Jan. 9) 1937.

²⁸ Sulzberger, M. B., and Goodman, J. Acquired Specific Hypersensitivity to Simple Chemicals. II. Cheilitis, with Special Reference to Sensitivity to Lipstick. *Arch. Dermat. & Syph.* **37** 597 (April) 1938.

²⁹ Baer, H. I. Lipstick Dermatitis. *Arch. Dermat. & Syph.* **32** 726-734 (Nov.) 1935.

(bromfluorescein derivatives) and 7 to a certain azo dye in the lipsticks, there was no sensitivity to methylheptene carbonate (perfume) in any case, in all cases benefit was obtained by the substitution of another lipstick of special formula. These same authors concluded that cheilitis due to lipstick is relatively rare and usually due to hypersensitivity to one or more of the dyes and pigments of the lipstick.

Sulzberger and Goodman cited from the French literature cases of marked eczematous hypersensitivity to hydrous wool fat.

In an important and extensive article, Baei²⁹ reported a case of lipstick dermatitis, with the aid of the manufacturer, he was able to test each of the ingredients, and methylheptene carbonate (a synthetic perfume derived from castor oil) was proved to be the offending agent. Baei conducted further studies of the perfume ingredient and found that of 38 women who used lipstick (without reaction) 50 per cent were sensitive to methylheptene carbonate and, further, that of 10 men, who did not use lipstick, 4 showed irritation from the perfume. Methylheptene carbonate is currently a widely used synthetic perfume.

Freudenthal¹⁶ reported a case of severe allergic disturbance of the upper part of the respiratory tract from the use of lip rouge.

NAIL POLISHES—COMPOSITION AND DANGERS

"Nail lacquers are solutions of nitrocellulose in various solvents, with the addition of certain aids to solution and plasticizers to make the film flexible"³⁰ Typical solvents are acetone, butyl acetate and amyl acetate, typical aids to solution, toluene, benzene, xylene and naphtha, and typical plasticizers, castor oil, camphor and rosin.

These preparations for the nails are apparently the least harmful of all the cosmetics, although minor disturbances of the nails are frequent. In general, the nails become brittle, and there is a splitting, characterized chiefly by the uplifting of scales of unequal keratin, principally at the tips of the nails. Acetic acid has been alleged, by certain authors, to be liberated from the lacquers and to cause the irritation,³⁰ it has also been stated that the injuries are due to the drying action of the solvents.

In an investigation of 25 cases (all in business women using the same brand of nail enamel), I found that nearly half of the group showed brittleness and splitting of the nails in some degree, strangely enough, the other half of the group were able to wear the polish without any sign of irritation.

³⁰ Nail Polishes and Lacquers, Queries and Minor Notes, J A M A **110** 1943-1944 (June 4) 1938

One case of leukoplakia due to nail enamel has been reported³¹ In another case of nail polish dermatitis, ethylene dichloride (the solvent) was found responsible³²

Hollander⁷ declared that nail paints and manicuring aids produce a scaling of the nail plates and occasionally an inflammation of the nail bed On the other hand, Downing^{3a} expressed the belief that liquid nail polishes may be of value by their antiseptic qualities in the prevention of infections that might have resulted from the none too sterile operating tools of the manicurist

HAIR DYES—COMPOSITION AND DANGERS

According to Carleton,¹¹ hair dyes include (1) vegetable dyes, such as henna, (2) metallic dyes, such as silver, copper, mercury, lead, nickel, cobalt and bismuth, in which the metal combines with the sulfur in the hair to form a deposit of metallic sulfide, (3) compounds of metallic salts and vegetable products, such as pyrogallol acid, and (4) aniline derivatives, of which the best known is paraphenylenediamine

Of all the cosmetics, the hair dyes are the worst offenders Not only are simple irritations reported throughout the literature from the use of hair dyes, but the most severe of systemic poisonings are reported and in an unusually large number of cases The story of poisoning by hair dye is not a new one

Many cases were reported in the latter part of the nineteenth century and throughout the early part of the current century Berger³³ in 1909 reported a case of temporary impairment of vision in a woman who had used a paraphenylenediamine-containing dye, the author cited several French authors to the effect that many severe cases of aniline dye poisoning from the use of hair dyes were being reported in the French literature

Three cases of dermatitis due to hair dyes containing paraphenylenediamine were reported by Knowles³⁴ in 1916 The author dealt with general considerations on the topic extensively

In the 111 cases of injury due to hair dye reported in the answers to the questionnaire cited previously⁹ such dangerous ingredients as lead acetate, sulfur and pyrogallol were found in the dyes, paraphenylenediamine was present in nineteen of the forty-one dyes tested

31 Greenbaum, S. S. Leukoplakia of Unusual Origin (Nail Enamel), *Arch Dermat & Syph* **33** 538 (March) 1936

32 Goodman, J., and Sulzberger, M. B. Acquired Specific Hypersensitivity to Simple Chemicals. I. Eczematous Sensitivity to Clothing and to Cosmetics, with Special Reference to Dyes. *J. Allergy* **9** 136-152, 1938

33 Berger, E. Visual Disturbance Due to the Use of Hair Dye Containing Aniline. *Arch Ophth* **38**:397-400 1909

34 Knowles, F. C. Dermatitis Caused by Cosmetics and Wearing Apparel Particularly Those Containing Paraphenylenediamine. *Pennsylvania M. J.* **19** 897-900, 1916

Miller and Taussig³⁵ reported 2 cases of severe dermatitis from the use of preparations containing aniline, in 1 case permanent baldness resulted six months later. In 3 cases from the British literature³⁶ severe systemic reactions were reported to be due to aniline hair dyes. A fourth report from the British literature³⁷ described a peculiar case of fatal asthma from the use of a hair preparation in a 40 year old man.

The consensus is that the reactions from aniline dyes are based on a hypersensitivity, which all persons have in some degree, to dyes containing paraphenylenediamine.

Hair tonics have been mentioned occasionally as a source of irritation, the offending ingredients are chiefly quinine, salicylic acid and resorcinol. Cole¹ reported 3 cases of severe reaction from the use of tonic, the offending ingredients were, respectively, lead, arsenic and salicylic acid. Gelfand³⁸ reported another case of dermatitis due to arsenic in a hair tonic.

Among cases of irritation due to preparations for the hair, dermatitis has been reported in 1 case³⁹ as due to quinine in a dandruff cream, in 1 case⁴⁰ perennial hay fever was attributed to lycopodium in a powder for oily scalp, and in another case⁴¹ an eruption was regarded as due to a shampoo.

Wave-setting preparations are mucilaginous substances which are used for producing or setting "natural" waves of the hair. Most of them consist of a mucilaginous gum, water and perfume, in several cases a reaction to such preparations has been reported in the literature. Hollander⁷ reported 3 cases of dermatitis due to a proprietary preparation (la gerardine), the offending ingredient of which could not be determined. A case of perennial hay fever has been reported⁴² as due to the karaya gum in a wave-setting fluid. Feinberg⁴³ reported an analogous case, in which persistent asthma was due to the karaya gum in a wave-setting fluid.

35 Miller, H E, and Taussig, L R. *Cosmetics*, J A M A **84** 1999-2002 (June 27) 1925

36 Injury from Hair Dye, *Medical News*, Brit M J **1** 373, 1922. Injury from Hair Dye, *Medicine and the Law*, *Lancet* **1** 1058, 1926. Nott, H W. Systemic Poisoning by Hair Dye, Brit M J **1** 421-422, 1921.

37 Oliver, T. Saturnine Asthma, *Lancet* **2** 907-909, 1922.

38 Gelfand, H H. Hypersensitiveness to Arsenic. Dermatitis from Liquid Arvon (Hair Tonic), *J Allergy* **7** 254-260, 1936.

39 Johnson, D W. Dermatitis Due to Application of Dandruff Cream, *Urol & Cutan Rev* **39** 173, 1935.

40 Lambright, G L, and Albaugh, R P. Perennial Hay Fever from Lycopodium. Report of a Case, *J Allergy* **5** 590-591, 1934.

41 Balyeat, R M. Cosmetic Dermatitis, *Northwest Med* **34** 12, 1935.

42 Bullen, S S. Perennial Hay Fever from Indian Gum (Karaya Gum), *J Allergy* **5** 484-487, 1934.

43 Feinberg, S M. Karaya Gum Asthma, J A M A **105** 505 (Aug 17) 1935.

EYELASH DYES—COMPOSITION AND DANGERS

Darkening of the eyebrows and eyelashes is accomplished in two ways, according to Greenbaum ⁴⁴ (1) by coating the hairs (with mascara or lamp black) and (2) by actually staining them (usually with a regular hair dye)

The "mild epidemic" of tragic reactions from the use of a proprietary preparation (lash-lure) early in the present decade is well known and has been widely reported in the literature

Bilateral necrosis of the cornea resulting from the use of lash-lure and leaving the user light perception only was reported by Moran ⁴⁵ The same result occurred in a case reported by McCally, Farmer and Loomis ⁴⁶ Three cases in which there was no serious impairment of vision have been described ⁴⁷

One case in which the termination was fatal was described by Forbes and Blake ⁴⁸ These authors were tremendously impressed with the severe systemic reaction to the paraphenylenediamine contained within lash-lure There was a possibility in this case that sepsis was the cause of death, the portal of entry being the ophthalmic lesions

PERFUMES—COMPOSITION AND DANGERS

Perfumes are of complex composition Baei ⁴⁹ stated

Animal perfumes, balsams and natural perfumes were utilized before the development of synthetic perfumes, these last are principally the esters, ketones and aldehydes of the coal tar products

Since the advent of synthetic perfumes there have occurred a large number of reactions to perfumes and to perfumed products Essentially, these reactions are characterized by a curious photopigmentation, described by many authors as "berlock dermatitis"

Two cases were reported by Goeckermann ⁴⁹ in 1922 In 1930, 5 additional cases were described by Gross and Robinson ⁵⁰

44 Greenbaum, S S Dermato-Conjunctivitis Due to Lash-Lure, an Eyelash and Eyebrow Dye, J A M A **101** 363-364 (July 29) 1933

45 Moran, C T Bilateral Necrosis of Cornea Following Use of Hair Dye on Eyebrows and Eyelashes, J A M A **102** 286-287 (Jan 27) 1934

46 McCally, A W, Farmer, A G, and Loomis, E C Corneal Ulceration Following the Use of Lash-Lure, J A M A **101** 1560-1561 (Nov 11) 1933

47 Bourbon, O Severe Eye Symptoms Due to Dyeing the Eyelashes, J A M A **101** 1559-1560 (Nov 11) 1933 Harner, C E Dermato-Ophthalmitis Due to the Eyelash Dye Lash-Lure, *ibid* **101** 1558-1559 (Nov 11) 1933 Jamieson, R C Eyelash Dye (Lash-Lure) Dermatitis with Conjunctivitis, *ibid* **101** 1560 (Nov 11) 1933

48 Forbes, S B, and Blake, W C Fatality Resulting from Use of Lash-Lure on Eyebrows and Eyelashes J A M A **103** 1441-1442 (Nov 10) 1934

49 Goeckermann, W H A Peculiar Discoloration of the Skin, J A M A **79** 605-607 (Aug 19) 1922

50 Gross, P and Robinson, L B Berlock Dermatitis Arch Dermat & Syph **21** 637-641 (April) 1930

In an interesting article in 1930 Lane and Strauss⁵¹ presented an extensive review of the subject and produced considerable evidence to point toward oil of bergamot as the offending ingredient and cause of this peculiar photopigmentation

Goodman⁵² described another case in 1931 and declared that "perfume dermatitis is probably more common than the rarity of its appearance in medical literature would indicate" Seven other cases in which oil of bergamot was considered the offending substance have been described by various authors⁵³

DEPILATORIES—COMPOSITION AND DANGERS

Carleton¹¹ stated

Barium sulphide is the commonest constituent of most depilatories, but sulphides of calcium, strontium, sodium or magnesium are also used, these appear to be generally harmless, but in sensitive skins, they may give rise to a generalized dermatitis

Thallium acetate was used in the past, but because of its intensely toxic action, it has more or less been discarded

Hollander⁷ expressed the belief that depilatories produce an indolent folliculitis which sooner or later becomes suppurative and then spreads by contiguity

"Koremlu" is a famous proprietary depilatory which rode to fame not on its beneficial effects but on the widespread destruction it caused its users Winters⁵⁴ declared in 1936

This product contained 7 per cent thallium acetate, a deadly poison commonly used to kill rats Baldness, skin injury, nervous and glandular troubles were some of the effects produced by Koremlu

VITAMINS IN COSMETICS

In the past few years a new phase has appeared in the development of cosmetics, namely, the introduction of preparations containing vitamins These are alleged to benefit the skin in various ways, from correcting "subnormal conditions of the skin" to "smoothing out the wrinkles and lines of old age"

51 Lane, J E, and Strauss, M J Toilet-Water Dermatitis with Especial Reference to "Berlock" Dermatitis, *J A M A* **95** 717-719 (Sept 6) 1930

52 Goodman, H Perfume Dermatitis, *Brit J Dermat* **43** 177-184, 1931

53 Downing, J G Pigmentation from Perfume Berlock Dermatitis, *New England J Med* **207** 660-662, 1932 Greenbaum, S S Cutaneous Photopigmentation and Cosmetics, with Special Reference to Berlock Dermatitis, *Pennsylvania M J* **38** 28-31, 1934 Tobias, N Emeraude Perfume Dermatitis, *J A M A* **104** 1322-1323 (April 13) 1935

54 Winters, S R Public Enemies No 1 Food, Drug and Cosmetic Racketeers, *Hygeia* **14** 832-835 (Sept) 1936

The use of vitamins in cosmetics will probably cause little if any harm, moreover, their efficacy will parallel their harmfulness. In 1937 *The Journal of the American Medical Association* discussed editorially⁵⁵ the complaint of the Federal Trade Commission against the manufacturer of a toilet soap containing vitamin D. Although the complaint was essentially against the fraudulent claims of the manufacturer, question was raised in the editorial whether vitamins exert any beneficial effect on the skin, even assuming the ability of the skin to absorb such substances.

PROTECTION OF THE COSMETIC CONSUMER

Fortunately for the consumer, the majority of cosmetics are relatively harmless. Most of these articles are useless as well. It is the protection of the consumer not from fraudulent and misbranded claims but from exposure to cosmetics which contain ingredients potentially dangerous to health with which this paper is concerned.

Aside from a few items of local legislation, principally against selected dangerous products, there were no restraints, federal, state or local, against the manufacture, sale or use of any cosmetic preparation until passage of the Federal Food, Drug and Cosmetic Act of 1938.

Intended to replace the Federal Food and Drug Act of 1906 (an act which failed to define cosmetics or include legislation against them), the new law was approved by the President on June 25, 1938, but it did not become wholly effective until June 25, 1939, in order to allow the various industries concerned time to conform with the provisions of the new act.

A report of the Bureau of Legal Medicine and Legislation of the American Medical Association^{55a} discloses most of the important provisions of the new act.

Cosmetics are defined by the new act as articles other than soap "intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance." Soaps that are represented as being of service in the cure, mitigation, treatment or prevention of disease come, however, within those provisions of the new act that relate to drugs.

Poisonous or deleterious ingredients are forbidden but only when it can be shown that they may render the cosmetic injurious to the user under the conditions of use prescribed in the labeling or under such conditions as are customary or usual.

⁵⁵ No Sunshine in Soap editorial, J A M A 109 509-510 (Aug 14) 1937

^{55a} The New Federal Food and Drug Act at Last editorial, J A M A 111 324-326 (Jul 23) 1938

Coal tar hair dyes are expressly permitted, except dyes for eyelashes or eyebrows, if cautionary statements are printed on the label. No ingredient of any kind need be disclosed on the label.

Any toilet article represented as having the power of preventing, mitigating or curing disease is, however, a "drug" within the meaning of the law and is subject to regulation as a drug.

Because of the broad provisions of the act as it pertains to cosmetics, its ability to protect the cosmetic consumer is doubtful and can be estimated only by actual trial. The outlawing of coal tar eyelash and eyebrow dyes is an excellent provision. The ruling against poisonous and deleterious ingredients, although vague, should help to reduce the incidence of injuries due to cosmetics.

It is somewhat unfortunate that the law does not require listing of ingredients on the label, because in this manner potentially dangerous substances would be known to the consumer and, secondarily, racketeering prices for ingredients of low actual cost would be reduced.

It should be remembered that the new law regulates cosmetics only in interstate and foreign commerce, which for the purposes of the law includes commerce within the District of Columbia and certain other exclusively federal jurisdictions. The cosmetic racketeer will still flourish in intrastate commerce unless the states themselves adopt the provisions of the Federal act or others at least equally effective.

The American Medical Association has accomplished much for the protection of the consumer, first, in investigating cases of actual injury from cosmetics and, second, in exposing fraudulent claims. The Bureau of Investigation of the American Medical Association publishes a pamphlet⁵⁶ devoted chiefly to the exposure of unscientific products.

It would seem moderately important, therefore, that the average physician and public health officer be aware of the nature and the potential dangers of the use of cosmetics, he may be consulted concerning injury from a cosmetic or asked the efficacy of some particular device. After reviewing the subject, I am amazed at the number and the variety of substances that persons expose themselves to in using the many cosmetic preparations.

Goodman,⁵⁷ in 1935, cited a case of dermatitis from a combination of two cosmetics, neither of which alone caused a reaction. It is surprising that more such occurrences have not been reported.

⁵⁶ *Cosmetics and Allied Preparations*, Bureau of Investigation, Chicago, American Medical Association, 1937.

⁵⁷ Goodman H. Skin Reactions to Combinations of Two Toilet Articles Neither of Which Alone Caused Irritation, *Arch Dermat & Syph* **32** 632 (Oct) 1935.

SUMMARY

Selected literature on the composition of and dangers in the use of important cosmetics (toilet powders, facial creams, lipsticks, nail polishes, hair and eyelash dyes, perfumes and depilatories) is reviewed briefly

Adequate statistics are lacking, but the incidence of severe injury from the use of cosmetics is relatively low in comparison with the number and the variety of cosmetics used

Earlier cosmetics frequently resulted in severe systemic poisonings (from lead mercury, etc), but the majority of injuries from cosmetics at the present time belong in the field of allergic dermatoses

The aniline dyes and coal tar derivatives, in particular the paraphenylenediamine group, are the most serious offenders Hair dyes, especially preparations for the eyelashes, are extremely dangerous I wonder how any person can put an unknown, foreign substance in close approximation to such an important structure as the eye

A new field of cosmetic manufacture, that of synthetic perfumes, is giving rise to many dermatoses Nail polishes, although relatively innocuous may cause extensive physical disturbance of the nails

Reference is made to the Federal Food, Drug and Cosmetic Act of 1938, designed to regulate interstate and foreign commerce in these items The new law defines cosmetics, outlaws ingredients proved to be deleterious or poisonous and rules against coal tar eyelash and eyebrow dyes Other coal tar dyes are permitted No cosmetic ingredient of any kind need be listed on the label

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LXXXVI—AN INQUIRY INTO THE CAUSE OF PEMPHIGUS

IS IT A VIRUS DISEASE?

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Chronic pemphigus vulgaris is a name used to identify a definite disease. Since the principal symptom and primary lesion of this disease is the appearance on the skin and mucous membranes of a number of uncomplicated blisters and since somewhat similar lesions may occur in other diseases, the diagnosis of pemphigus is often a confusing problem in certain cases. There are borderline cases in which dermatitis herpetiformis, erythema multiforme, lupus erythematosus and even certain general infections of the blood stream may be accompanied by numerous bullae and may run a course simulating pemphigus to such a degree that in the absence of other than clinical criteria differentiation is almost a matter of personal opinion or even guesswork. Such cases are relatively rare, but there is a sufficient number of them in the experience of most dermatologists to color the general concept of just what pemphigus is and where it should be placed in the classification of diseases. In a recent European symposium on pemphigus, the chronic vulgaris type was generally identified as a separate and distinct disease.¹

In the last few years knowledge of filtrable viruses in general has been increasing, and new methods of demonstrating viruses have been devised. Certain diseases previously of unknown cause have been shown to be due to filtrable viruses. For these reasons, one of us (F S M) has been devoting his time to a study of a number of cutaneous diseases of unknown origin in an attempt to find and demon-

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Studies, observations and reports from the Dermatological and Research Departments of the Barnard Free Skin and Cancer Hospital, service of Dr M F Engman Sr.

1 Du Bois, C. Comment se faire une opinion sur le probleme des pemphigus d'apres l'observation clinique, *Schweiz med Wchnschr* 68 777, 1938, abstracted, Wise F, and Sulzberger, M B. Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1938, p 167.

strate filtrable viruses. In the course of this work special effort was devoted to a study of pemphigus vulgaris. Seven typical cases were investigated.

The method chosen in the present investigation has been the technic of chick embryo inoculation as developed by Goodpasture² and his colleagues for the study of filtrable viruses and other infectious agents. The chick embryo with its enveloping membranes offers three outstanding advantages as an experimental medium. First, perhaps because of their high metabolic and growth rates, embryonic tissues have a marked degree of susceptibility to virus infection. To date some twenty-five or thirty viruses have been cultivated in the developing chick, and to the majority of these infectious agents the adult chicken is completely resistant. Thus, to a considerable degree it is possible by the use of embryonic tissues to overcome the experimental difficulties imposed by the more or less specific host requirements of many parasitic micro-organisms. Second, embryonic tissues are for the most part sterile. Certainly they are free from the great variety of parasites which compose the normal flora of the body surfaces and cavities of the adult animal. Because of this sterility, one has a reasonable degree of assurance that the infectious agents isolated from inoculated embryos were those experimentally introduced and not some already resident in the tissues at the time of injection. Finally, from the dermatologic point of view, there is the advantage of having in the chorioallantoic membrane a readily available ectodermal tissue for experimental inoculation. In addition to working with the developing egg, we have employed, with or without modification, some of the methods used by other investigators in the study of pemphigus in experimental animals.

REPORT OF CASES

CASE 1—R. K., a white woman 76 years of age, was observed and treated in the Barnard Free Skin and Cancer Hospital for about ten months. Over the entire body and in the mouth there was a diffuse bullous eruption typical of pemphigus vulgaris. The results of laboratory and other examinations were not remarkable. The patient recovered after prolonged treatment with injections of iron cacodylate and with blood transfusions. She has remained well for a year.

CASE 2—M. B., a white woman 49 years of age, entered Barnard Hospital March 22, 1938, suffering from typical pemphigus vulgaris of eleven months' duration. The results of laboratory and other examinations were not remarkable. The patient died of terminal bronchopneumonia June 25, 1938.

CASE 3—M. K., a white woman 28 years of age, was admitted to the Jewish Hospital May 24, 1938, suffering from a severe bullous eruption over the body and in the mouth. She did not improve with any treatment and died Oct. 18, 1938. Since in addition to the bullae over the body there was also foul-smelling vegetation in the axillae a diagnosis of pemphigus vegetans was made. She died of pemphigus.

² Goodpasture, E. W. Some Uses of Chick Embryo for the Study of Infection and Immunity. *Am. J. Hyg.* 28:111, 1938.

CASE 4—G S, a white man 65 years of age, was admitted to the Jewish Hospital on June 1, 1938, suffering from generalized severe bullous eruption of six months' duration. A diagnosis of pemphigus vulgaris was made. The patient remained in the hospital under observation and treatment for about three months. His treatment consisted mainly of injections of iron cacodylate. At the time of his discharge he was improved.

CASE 5—A N, a white woman 28 years of age, was admitted to the Jewish Hospital on Oct 16, 1938, and remained only four days. She had a generalized bullous eruption of three months' duration. A diagnosis of pemphigus was concurred in by most of the dermatologists who examined this patient. However, there was some difference of opinion, and the possibility of bullous erythema multiforme was not ruled out in the opinion of some observers.

CASE 6—E M, a white woman 60 years of age, had a vesicubullous eruption which began six months before she entered the Barnard Free Skin and Cancer Hospital. At the time of entry the patient was suffering from a well developed profuse bullous eruption typical of pemphigus vulgaris. The results of laboratory and other examinations were not remarkable. The phytopharmacologic index was 66 per cent in October 1938 and 43 per cent in January 1939.

CASE 7—B Y, a white woman 46 years of age, entered Barnard Hospital in January 1939, suffering from generalized pemphigus vulgaris of one year's duration. She remained in the hospital under observation and treatment for two months and then left under protest. The results of laboratory and other examinations were not remarkable.

REPORT OF EXPERIMENTS

EXPERIMENT 1—Eggs incubated for nine to twelve days at 38 C in a commercial incubator were opened by removing a small square of the shell and shell membrane. Onto the exposed chorioallantois, from 0.2 to 0.3 cc of inoculum was dropped from a 1 cc tuberculin syringe. The shell opening was closed by ringing it with a sterile mixture of petrolatum and paraffin and placing over it a sterile cover glass. The inoculated eggs were then placed in a bacteriologic incubator and held at 35 C for four to ten days. The eggs were examined from time to time for evidence of infection.

From three to six eggs were inoculated with blister fluids, either unfiltered or as Berkefeld V filtrates, from all 7 patients with pemphigus, which were removed as soon as possible onto the chorioallantoic membrane of the developing egg. Similarly, from three to six control eggs were inoculated with blister fluid heated to 60 C for thirty minutes. As a result, although some of the specimens were carried through several passages on the chorioallantoic membrane, none of the fluids from any of the 7 patients gave rise to lesions or changes in the membrane which differed in any way from those observed in the control eggs. Normal chicks hatched from eggs which were allowed complete development.

EXPERIMENT 2—In order to overcome the possible inhibiting effect of antibodies contained in the blister fluid, decimal dilutions to 1:100,000 were prepared by the addition of physiologic solution of sodium chloride to the blister fluid. Two eggs were inoculated with each dilution. The results were the same as those obtained with undiluted blister fluid.

EXPERIMENT 3—From 1 patient (case 1), 0.5 cc of unfiltered blister fluid was injected intracerebrally into each of 2 rabbits, and approximately 0.25 cc was instilled into the conjunctival sac after scarification of the cornea with a sharp needle. 0.03 cc of the fluid was injected intracerebrally into each of 6

white mice (Buffalo strain) The same fluid in the form of a Berkefeld V filtrate was similarly injected into 2 rabbits and 6 mice Seven weeks after inoculation snuffles developed in 1 of the rabbits inoculated with the unfiltered blister fluid, and it died No lesions were found on gross or microscopic examination of its brain One of the mice inoculated with the same specimen died five days after the injection A large abscess in the liver was noted post mortem, but on microscopic examination the brain and kidneys were observed to be free of lesions No vesicles or ulcerations appeared on the scarified corneas of the rabbits, and all the remaining animals continued symptomless during an observation period of four months

EXPERIMENT 4—Twenty-six young white mice were placed in a pasteboard box which was approximately 3 cm deep and provided with a cellulose acetate window in the lid The mice were exposed to 400 r of roentgen irradiation Immediately, each of 3 males and 4 females was inoculated intracerebrally with 0.03 cc of unfiltered blister fluid from a patient (case 6) Three males and 4 females were similarly inoculated with unfiltered fluid from a patient (case 7) The remaining 4 males and 8 females were intracerebrally inoculated with the combined blister fluids from the 2 patients after the mixture had been heated to 60 C for a period of thirty minutes One of the males inoculated with unheated blister fluid from a patient (case 7) was found dead of wounds on the eighth day A second badly wounded male was etherized, and the brains of both were prepared for histologic examination Neither brain showed any evidence of meningitis or encephalitis All of the controls and the remaining test animals of both groups were vigorous and without symptoms at the end of eight weeks' observation

EXPERIMENT 5—Blister fluid and blood serum from 2 patients (cases 1 and 2) were injected in amounts varying from 0.1 to 0.5 cc in separate sites into the shaven skin of rabbits As a result, a slight inflammatory response occurred at the points of injection, but the reaction rapidly faded, and no bullae or other cutaneous vesicles appeared on the skin of either rabbit

EXPERIMENT 6—Bacteriologically sterile blister fluid from 1 patient (case 2) was set up in 1 cc amounts in plasma clot cultures of minced 8 day old chick tissue One cubic centimeter of a 25 per cent concentration of normal rabbit serum was added to each culture Control cultures were similarly set up with normal rabbit serum in place of the pemphigus blister fluid As a result, although the cultures were periodically examined for several days, no appreciable differences in the rate, amount or character of the growth of the tissues in the two sets of cultures could be observed Examination of fixed and stained sections of the cultures revealed nothing of significance

COMMENT

It is our present opinion that pemphigus vulgaris is not caused by a filtrable virus There is a considerable weight of evidence which points to this conclusion

Contagion—In virus diseases characterized by the formation of vesicles, pustules or bullae—such as herpes simplex, varicella, variola, foot and mouth disease or vesicular stomatitis—the virus is abundantly present in the vesicles If pemphigus were a virus disease, it would seem likely that the fluid from the bullae would contain an abundance

of living virus and that, since special precautions are seldom observed in handling patients with pemphigus, susceptible persons would be exposed to the virus and would acquire the disease. So far as we are aware, however, there is no report of any doctor, nurse or other person so exposed ever acquiring pemphigus vulgaris from a patient.

Experimental Work—The various attempts reported in this paper to demonstrate a virus pemphigus gave negative results. It might be mentioned, in view of these negative results, that there are virus diseases in which such a high degree of host specificity exists that no experimental animal can be successfully used to demonstrate the virus other than the natural host. Therefore, the negative results of these experiments do not actually rule out the possibility of a pemphigus virus. However, they add to the sum total of evidence against the hypothesis that pemphigus is a virus disease.

Following the report of Urbach and Reiss,³ there have appeared in the recent literature numerous papers dealing with the virus etiology of pemphigus. Some of the evidence presented in these publications confirms the work of Urbach and his collaborators, and about an equal amount fails to do so. On analysis of the evidence so far presented, it is our opinion that sufficient proof has not been offered to establish a virus as the cause of pemphigus.

While there is still much to be learned about the nature and properties of filtrable viruses, knowledge of them at present is considerable. Because a disease is of unknown causation, that disease is not ipso facto a virus disease. Koch's postulates are as valid for virus infections as for those caused by bacteria. There are few broad generalizations that can be made about filtrable viruses, for they are as diverse in their characteristics as are protozoa, bacteria and fungi. They vary greatly in their range of hosts, in the nature of the lesions which they excite, in the manner of their transmission and in the degree and duration of the immunity which they confer.

In the laboratory, viruses cannot be cultivated in the sterile environment of artificial mediums. This fact requires that viruses be passed from animal to animal, a necessity that is fraught with a certain degree of risk, for laboratory animals as well as man have their quota of viruses and other parasites. It is therefore essential that research on viruses be undertaken with a full knowledge of the spontaneous infections likely to be encountered in experimental animals. Histologic examination of tissues with careful attention to cytologic detail and

3 Urbach, E., and Reiss, F. Tierexperimentelle Untersuchungen zur Frage der infectiostovischen Genese des Pemphigus vulgaris und der Dermatitis herpetiformis Duhring, Arch f Dermat u Syph 162 713 1930

frequent immunologic checks are needed if the hazards of spontaneous infections are to be recognized and avoided

With the exception of the work of Grace and Suskind,⁴ most of the experimental inoculations with pemphigus materials have been made in rabbits. It is well known that these animals are prone to infection with a protozoan parasite, *Encephalitozoon cuniculi*, and that latent infections of the central nervous system may be lighted up by intracerebral inoculations with foreign material or even by simple puncture. This parasite is cosmopolitan in distribution, and most stocks of domestic rabbits become infected at one time or another. The presence of *E. cuniculi* is not revealed by aerobic or anaerobic cultural methods, and the organism is readily transmitted serially from brain to brain. Hence, the unwary investigator may be led to believe that he is dealing with a virus etiologically related to the disease under investigation. If filtrates fail to transmit the disease as readily as crude tissue emulsions, it is natural to invoke the well known facts that some viruses filter with great difficulty and that the process of filtration may greatly reduce the amount of virus in potent emulsions.

In spite of its name, *E. cuniculi* is primarily a kidney parasite. This fact was brought out by the work of Smith and Florence⁵ and by the earlier observations of Twort and Archer,⁶ who believed that they were dealing with a nephritis caused by a filtrable virus. The latter investigators described the symptoms, the lesions in the brain, the progressive cachexia and even the alopecia which constitute the current syndrome of experimental pemphigus in the rabbit. (In the years immediately following the World War, these same manifestations were thought to characterize human lethargic encephalitis in the rabbit.) In 1924, Da Fano⁷ reviewed the literature concerning spontaneous encephalitis in rabbits and pointed out a number of instances in which this protozoan infection had led to confusion and erroneous conclusions on the part of investigators who failed to recognize the disease.

It seems likely that the agent described by Grace and Suskind⁴ also belongs in the category of spontaneous infections, although it is clear that they are not dealing with the protozoan parasite studied by Cowdry.

4 Grace, A. W., and Suskind, F. H. An Agent Transmissible to Mice Obtained During a Study of Pemphigus Vulgaris, *Proc Soc Exper Biol & Med* **37**:324, 1937.

5 Smith, T., and Florence, L. *Encephalitozoon Cuniculi* as a Kidney Parasite of the Rabbit, *J Exper Med* **41**:25, 1925.

6 Twort, C. C., and Archer, H. E. The Experimental Production of a Fatal Nephritis with a Filter Passing Virus of Nervous Origin, *Lancet* **1**:1102, 1923.

7 Da Fano, C. Spontaneous and Experimental Encephalitis in Rabbits. *Science* **10**:355, 1924. Protozoan-like Parasites in Spontaneous Encephalitis of Rabbits. *J Pathol & Bact* **27**:333, 1924.

and Nicholson⁸ which closely resembles or is identical with E. cuniculi. Grace⁹ has stated the belief that his virus is not the same as that described by Urbach and that rabbits are unaffected by the agent which he isolated from mice. In the discussion of their most recent publication, Grace and Suskind⁹ stated that mice recovered from infection were not found to be resistant to reinfection by the same agent. This is the only immunologic work they have reported. They apparently have not attempted neutralization tests with pemphigus patients' serum to establish some relationship between their virus and the human disease. The agent with which they are dealing appears to be decidedly pyogenic. This property is in no way reflected in the pathologic changes of human pemphigus. On the other hand, the massive polymorphonuclear infiltrations in their mice are suggestive of the action of a virus recently described by Woglom and Warren¹⁰. This virus was isolated from rats, but it is also pathogenic for mice^{10a}.

In the writings of Urbach and Wolfram,¹¹ considerable emphasis is laid on the suboccipital route of inoculation. While this method may offer certain advantages, these are largely offset by the opportunity it presents for serious trauma. Moreover, it would seem improbable that virus introduced directly into nerve tissue by cerebral injection would fail to infect whereas it would do so if inoculated suboccipitally into the dural spaces. By either method, most of the inoculum doubtless finds its way into the cerebrospinal fluid. Fleck and Goldschlag^{12a} recently reported an interesting experiment in which they had the opportunity to observe the effects of trauma under what might be called optimum conditions. Since they were dissatisfied and unconvinced by the results of their own inoculations, Dr. Wolfram volunteered to

8 Cowdry, E. V., and Nicholson, F. M. Coexistence of Protozoan-like Parasites and Meningoencephalitis in Mice, *J. Exper. Med.* **40** 51, 1924, Meningoencephalitic Lesions and Protozoan-like Parasites in Brains of Apparently Normal Laboratory Animals Commonly Employed for Experimentation, *J. A. M. A.* **82** 545 (Feb. 16) 1924.

9 Grace, A. W., and Suskind, F. H. An Investigation of the Etiology of Pemphigus Vulgaris. The Isolation of a Transmissible Agent from a Fourth Case of the Disease, *J. Invest. Dermat.* **2** 1, 1939.

10 Woglom, W. H., and Warren, J. A Pyogenic Virus in the Rat, *Science* **87** 370, 1938.

10a Since this paper was submitted for publication it has been discovered that this filtrable agent is a cultivable micro-organism belonging to the bovine pleuropneumonia group.

11 Urbach, E., and Wolfram, S. Virus of Pemphigus and Dermatitis Herpetiformis, *Arch. Dermat. & Syph.* **33** 788 (May) 1936.

12 Fleck, L., and Goldschlag, F. (a) Further Experimental Studies on Pemphigus, *Brit. J. Dermat.* **51** 70, 1939, (b) Experimentelle Beiträge zur Pemphigusfrage, *Klin. Wchnschr.* **16** 707, 1937.

perform the injections for them at the Lwów Clinic. Thirty-four rabbits were inoculated, and 23 of these rabbits received normal blood serum or other material of nonpemphigus origin. In 3 animals among the pemphigus test group and in exactly the same number among the controls Urbach's paralysis developed, and they died. Postmortem examination of the controls revealed unmistakable evidence of trauma to neural and vascular tissue in the region of the fourth ventricle. Fleck and Goldschlag came to the conclusion that this method of inoculation is a dangerous one and that animals may die as a result of trauma several days after the inoculation is made. Since Urbach and Wolfiam regarded the death of any animal forty-eight or more hours after inoculation as resulting from pemphigus virus infection, their high percentage of successful inoculations becomes more understandable.

In addition to animal transmission experiments, Urbach and his colleagues have offered a certain amount of serologic and immunologic evidence designed to show the relationship of their virus to human pemphigus and to other viruses. Although Urbach, Wolfiam and Brandt¹³ described a complement fixation reaction which appeared to have prognostic as well as diagnostic value, Fleck and Goldschlag¹⁴ found that the test was lacking in specificity, since 25 per cent of syphilitic serums gave a positive reaction with the antigen prepared by the Viennese investigators. Moreover, they observed that serums giving a positive reaction with the pemphigus rabbit brain antigen reacted in the same manner with phenolized normal rabbit brain as well as with phenolized starch or malt solutions.

The relationship of rabies virus to Urbach's rabbit pemphigus virus, described by Schweinberg and Wolfram,¹⁴ is unconvincing. Their published protocols show that not only did serums from patients with pemphigus and dermatitis herpetiformis neutralize their rabies virus but so did their control serums from patients with herpes zoster, erythema exudativum multiforme, mycosis fungoides, erythema annulare and Daniel's disease. A strain of rabies virus susceptible to neutralization by serums from such diverse sources is certainly of doubtful value in establishing serologic relationships.

Our single experiment using pemphigus blister fluid as a major part of the medium in the culture of chick tissues has a bearing not only on the possible infectious nature of pemphigus but also on the validity of the Pels-Macht test. It would seem reasonable to suppose that a specific

13 Urbach, E. Wolfram, S. and Brandt, R. Zur Serodiagnose des Pemphigus, *Klin Wchnschr* **15** 1479, 1936.

14 Schweinberg, F., and Wolfram, S. Ueber serologische und immunologische Beziehungen zwischen den Erregern des Pemphigus und der Lassa. *Ztschr f Immunitätsforsch u exper Therap* **91** 341 1937.

substance of mammalian origin sufficiently toxic to inhibit the growth of a plant seedling would also have a decidedly toxic effect on naked animal cells growing in tissue culture. On the contrary, our cultures containing relatively high concentrations of blister fluid grew as luxuriantly as did those in normal rabbit serum. On statistical grounds, Sansome and Forman¹⁵ and Hollander and Greb¹⁶ have also cast doubt on the validity of the phytopharmacologic test of Pels and Macht in the diagnosis of pemphigus.

SUMMARY AND CONCLUSIONS

Experiments are described in which it was attempted to demonstrate the presence of a filtrable virus in pemphigus blister fluid by the inoculation of the chorioallantoic membrane of the developing chick and by intracerebral inoculation of rabbits and irradiated mice. The results were entirely negative.

On the basis of clinical and experimental data, it is concluded that there is insufficient evidence at present to justify the theory that a virus is the cause of pemphigus vulgaris.

15 Sansome, F. W., and Forman, L. A Note on the Phytopharmacological Index in Pemphigus, *Brit J Dermat* **51** 63, 1939.

16 Hollander, L., and Greb, R. J. Evaluation of the Phytopharmacologic Test of Pels and Macht, *Arch Dermat & Syph* **33** 1012 (June) 1936, Further Report, *ibid* **34** 650 (Oct) 1936.

ABSORPTION OF ROENTGEN RAYS BY THE SKIN

EXPERIMENTAL DETERMINATIONS

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The biologic effect of roentgen irradiation depends on absorption of the rays applied to the site of the pathologic process. In different cutaneous lesions this site is situated at different levels in the skin and subcutaneous tissues, hence it is necessary to determine the optimal quality and quantity of radiation to use in each specific case. It was therefore deemed advisable to determine the amount of radiation of the qualities used in dermatologic practice which is absorbed in successive millimeters of skin.

MATERIAL AND METHOD

Determinations of absorption were made with live and dead rabbit skin, ear and thigh, fresh human skin obtained from the operating room, water and aluminum. Our measurements were all made in air, to avoid the effect of scattering. The apparatus used was a mechanical rectifier with a universal type Coolidge tube. The peak kilovoltage was 100, the milliamperage was 3 and the skin focal distance was 50 cm, with a portal 3 by 3 cm.

Since the amount of scattering is dependent on many factors, we attempted to determine to what degree the freely circulating blood influences scattering. A white rabbit was securely tied to a board, and the hair was clipped from an area measuring 9 by 9 cm. A double thickness of skin was held together with clamps, measured and exposed to a beam of roentgen rays. The dose delivered to the surface was 57 r per minute. The same dose was applied to the ear and to the fleshy part of the thigh, and in each case the transmitted portions of the roentgen beam were measured. The animal was then anesthetized, and a flap of skin was cut sufficiently large to cover the ionization chamber. There was no interference with the free circulation of the blood. A reading was taken, and the thickness of the skin was measured with a micrometer. Finally the animal was anesthetized and killed, the flap of skin was removed and the ear and thigh were severed. The amount of radiation absorbed by these dismembered parts was measured. The experimental conditions and the thicknesses of the test materials were not altered.

We were interested only in comparing the absorption by live and by dead tissues, so that the effect of circulation could be definitely determined. Table 1 clearly indicates negligible difference in absorption between live and dead tissues. The conclusion is justifiable that for small thicknesses and for small areas the

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amount of absorption of a low voltage x-ray beam is not measurably influenced by normal circulation

The absorption of radiation in human skin was next determined. The same factors, apparatus and conditions were used for these experiments as for those with animal tissues. Having determined that freezing of human skin with solid carbon dioxide has no effect on absorption of the roentgen rays, we cut the skin in thicknesses of 1 mm. Fresh human skin was obtained from the operating room. Care was taken to prevent evaporation of water. Not only was the subcutaneous tissue separated from the skin, but the cutis was cut away from the epidermis. The thickness of the skin and that of the fat were measured by placing each on a glass slide and placing another slide carefully over the surface of the material. The thickness of the specimen minus that of the slides was determined with a micrometer. We thought that this would be more accurate for our purpose than weighing a known area. The skin, cut into convenient sizes, was placed over a piece of lead foil having an appropriate opening. A tripod was used to support the lead foil and the sample in such a way that the x-ray tube was directly over, and the ionization chamber directly below, the skin. Absorption readings obtained

TABLE 1—*Relative Transmission of Low Voltage Unfiltered Roentgen Rays in Live and in Dead Animal Tissue*

| | Thickness
of Tissue | Dose Applied
to Surface,
r/Min in Air | Trans-
mission
in Live
Tissue,
r/Min | Trans-
mission
in Dead
Tissue,
r/Min |
|---------------------------------|------------------------|---|--|--|
| Double thickness of rabbit skin | 3.6 mm | 57 | 31.2 | 31 |
| Rabbit skin flap | 1.7 mm | 57 | 42 | 41.4 |
| Rabbit ear | 1.2 mm | 57 | 45.2 | 44.8 |
| Rabbit thigh | 3.3 cm | 57 | 11 | 11 |

with varying thicknesses of human skin and fat were compared with those obtained with rabbit skin, water and aluminum. These data appear in table 2 and figure 1.

It is interesting to note that the skin absorbs a greater percentage of the incident beam than does its underlying subcutaneous tissue or water. However, when averages of the absorption readings for fat and skin are obtained, pooled and compared with those for water the difference is negligible. There is general agreement that the density of water and that of human tissues are about the same, and therefore experimental results obtained with a water phantom apply to human tissues. In this study, clipped rabbit skin absorbed more radiation than did human skin or water.

In order to measure the degree of absorption of an x-ray beam by successive small thicknesses of water, an apparatus was devised for this purpose. If we had placed an ionization chamber in a water tank as one would do in performing water phantom experiments, the interference by scattering would have been so great as to invalidate our results for comparison. The cylinder and plunger arrangement shown in figure 2 was utilized. The plunger was attached by a side arm to a set screw which measured 12 full turns per centimeter of plunger motion. Therefore, each turn of the set screw increased by 0.83 mm the column of water which the roentgen rays had to traverse. The cylinder and plunger were made of bakelite tubes with paper across the bottom which was stiffened and waterproofed with a cellulose cement. This paper absorbed only about 2 per cent of the incident beam, but the water which seeped under the plunger absorbed about 15 per cent. A reading was obtained with each successive turn of the set screw. The data are shown in table 3.

The device was supported on a tripod with the x-ray tube above it. The diaphragm emitted a pencil of rays which traversed the hollow plunger and the column of water beneath it and finally struck the ionization chamber placed

TABLE 2—*Comparative Absorption of Low Voltage Unfiltered Roentgen Rays in Varying Thicknesses of Different Materials*

| Human Skin | | Human Fat | | Rabbit Skin | | Water | | Aluminum | |
|------------|-------|-----------|-------|-------------|-------|-------|-------|----------|-------|
| Mm | r/Min | Mm | r/Min | Mm | r/Min | Mm | r/Min | Mm | r/Min |
| 0 | 45.2 | 0 | 44.4 | 0 | 57 | 0 | 38 | 0 | 61.8 |
| 2.0 | 33.6 | 10 | 21.6 | 1.7 | 42 | 2.5 | 28 | 1 | 25.2 |
| 4.25 | 25.2 | 18 | 14.8 | 3.6 | 31.2 | 5.0 | 23.6 | 2 | 17.6 |
| 6.40 | 21.2 | 26 | 12.0 | | | 7.5 | 20.7 | 3 | 15.0 |
| 8.35 | 17.6 | | | | | 10.0 | 18.0 | 4 | 12.0 |
| | | | | | | 12.5 | 15.9 | 5 | 11.0 |
| | | | | | | 15.0 | 14.5 | 6 | 9.6 |

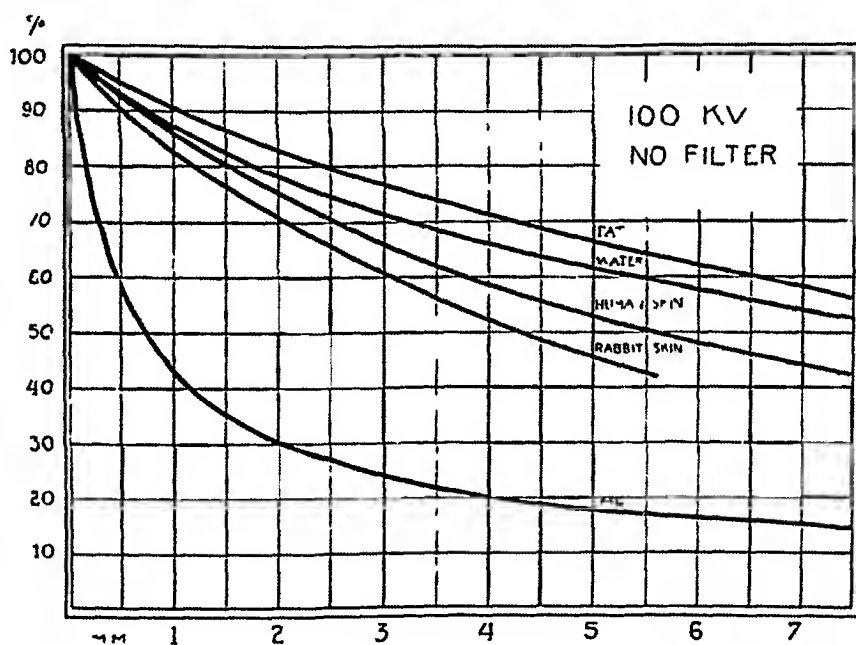


Fig 1—Curves representing absorption by various test materials used in our experiments of roentgen rays with unfiltered radiation at 100 kilovolts

beneath the water device. This arrangement eliminated scattering for the most part.

Absorption curves for aluminum were obtained in the conventional manner, whereby primary absorption only is measured. It was our aim to measure all data under equal conditions in order to permit direct comparison of the absorption measurements through various substances.

So far we have determined (1) that there is a negligible difference in absorption between live and dead tissue that has not been subjected to loss of fluid, (2) that there is a definite difference in absorption between rabbit and human skin and that this difference can be calculated mathematically, and (3) that there is agreement in absorption readings between skin with its subcutaneous tissue and water. These experiments open the way to further and more accurate studies on the absorption of roentgen rays in minute thicknesses of cutaneous structures.

The next phase of the study was concerned with the relative absorption of rays of different qualities by water and by human skin. Aluminum was used both as a control and for comparative purposes. Absorption curves were made with the irradiation factors previously described, and human skin, water and aluminum were used as filtering materials. The rays used were grenz rays (10 kilovolts) 40, 60, 80, 100 and 115 kilovolts peak, with 3 milliamperes and no filtration, also 137 kilovolts peak, with 5 milliamperes and a 3 mm aluminum filter. The data are recorded in table 4, and curves obtained from these figures are illustrated in figure 3. It is interesting to note that the higher the voltage

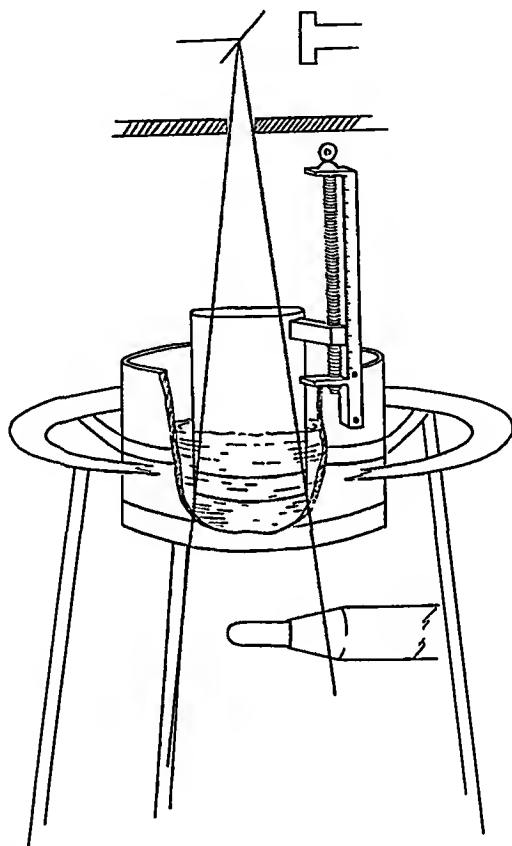


Fig 2—Diagram of the apparatus used for measuring the transmission of roentgen rays through water. The tripod holding the device, the relative positions of the x-ray tube, the diaphragm and the ionization chamber are also indicated.

and filtration the greater the transmission of the x-ray beam through skin, water and aluminum. The reverse is true for the lower voltages.

The figures obtained in the absorption experiments were plotted on semi-logarithmic graph paper. The purpose of these graphs was to show more specifically the absorption quality of the test materials (human skin, water and aluminum) and also to compare the relative depths of penetration of radiations of varying qualities (10 to 140 kilovolts peak). The results are shown in figure 4.

Thus, the half value layer for 100 kilovolts peak with no filter in skin is about 57 mm, whereas in water it is 8 mm and in aluminum it is about 0.7

mm It can therefore be said that the amount of absorption for low voltage radiation in aluminum is approximately ten times that in water Meyer has repeatedly pointed this out The same relative differences are seen with other voltages

TABLE 3—*Relative Absorption of Low Voltage Unfiltered Roentgen Rays in Varying Heights (Thicknesses) of Water*

| Material | Absorption,
r/Min | Material | Absorption,
r/Min |
|----------------|----------------------|-----------------|----------------------|
| Air | 47.0 | Water—Continued | |
| Paper | 46.0 | 12 turns | 18.0 |
| Water (scaped) | 38.0 | 13 turns | 17.1 |
| 1 turn* | 33.6 | 14 turns | 16.8 |
| 2 turns | 30.0 | 15 turns | 15.9 |
| 3 turns | 28.0 | 16 turns | 15.4 |
| 4 turns | 27.2 | 17 turns | 15.2 |
| 5 turns | 25.2 | 18 turns | 14.5 |
| 6 turns | 23.6 | 19 turns | 14.0 |
| 7 turns | 22.5 | 20 turns | 13.7 |
| 8 turns | 21.0 | 21 turns | 13.4 |
| 9 turns | 20.7 | 22 turns | 13.0 |
| 10 turns | 19.2 | 23 turns | 12.6 |
| 11 turns | 18.6 | 24 turns | 12.4 |

* Turns of the set screw in the apparatus shown in figure 2. At each turn the column of water to be traversed by the roentgen rays was increased by 0.83 mm

TABLE 4—*Relative Difference in Absorption of Roentgen Rays with Radiations from 10 to 137 Kilovolts Peak in Human Skin, Water and Aluminum **

| | 10 Kv
(Grenz) | | 40 Kv | | 60 Kv | | 80 Kv | | 100 Kv | | 115 Kv | | 137 Kv
(5 mm and
3 mm Al) | |
|----------|------------------|-------|-------|-------|-------|-------|-------|-------|--------|-------|--------|-------|---------------------------------|-------|
| | Min | r/Min | Min | r/Min | Min | r/Min | Min | r/Min | Min | r/Min | Min | r/Min | Min | r/Min |
| Skin | 0 | 324 | 0 | 98 | 0 | 22.0 | 0 | 34.8 | 0 | 45.2 | 0 | 54 | 0 | 16.4 |
| | 1.05 | 78.0 | 4.06 | 4.3 | 4.06 | 10.6 | 4.06 | 18.5 | 2.0 | 38.6 | 3.01 | 35 | 4.06 | 14.7 |
| | 1.43 | 40.0 | 7.61 | 2.8 | 7.61 | 7.5 | 7.61 | 13.7 | 4.25 | 25.2 | 5.93 | 25 | 7.61 | 13.5 |
| | 2.46 | 3.0 | 11.23 | 1.95 | 11.23 | 5.5 | 11.23 | 10.6 | 6.40 | 21.2 | 9.20 | 18.5 | 11.23 | 12.4 |
| | 4.94 | 0.7 | 13.72 | 1.60 | 13.72 | 4.5 | 13.72 | 8.9 | 8.35 | 17.6 | 13.13 | 16.0 | 13.72 | 11.7 |
| Water | 0 | 112 | 0 | 7.0 | 0 | 17.2 | 0 | 28.8 | 0 | 38 | 0 | 45 | 0 | 16.8 |
| | 0.83 | 2.8 | 5.0 | 3.3 | 5.0 | 8.8 | 5.0 | 15.2 | 5.0 | 23.6 | 5.0 | 31.5 | 5.0 | 15.6 |
| | 1.66 | 0.95 | 10.0 | 2.1 | 10.0 | 5.7 | 10.0 | 10.5 | 10.0 | 18.0 | 10.0 | 22.7 | 10.0 | 14.0 |
| | 2.49 | 0.6 | 15.0 | 1.4 | 15.0 | 4.2 | 15.0 | 8.2 | 15.0 | 14.5 | 15.0 | 18.4 | 15.0 | 12.6 |
| | 3.32 | 0.3 | 20.0 | 1.15 | 20.0 | 3.2 | 20.0 | 6.4 | 20.0 | 12.4 | 20.0 | 15.2 | 20.0 | 11.7 |
| Aluminum | 0 | 324 | 0 | 98 | 0 | 22.0 | 0 | 34.8 | 0 | 45.2 | 0 | 57 | 0 | 16.5 |
| | 0.25 | 1.2 | 0.25 | 4.8 | 0.25 | 11.6 | 0.25 | 20.0 | 0.25 | 39.6 | 0.25 | 35 | 0.25 | 16.0 |
| | | | 0.50 | 3.0 | 0.50 | 8.0 | 0.50 | 15.4 | 0.5 | 32.4 | 0.5 | 27 | 0.50 | 15.2 |
| | | | 0.75 | 2.5 | 0.75 | 6.4 | 0.75 | 12.2 | 1.0 | 25.2 | 1.0 | 22 | 0.75 | 14.2 |
| | | | 1.0 | 1.7 | 1.0 | 4.9 | 1.0 | 10.4 | 2.0 | 17.6 | 2.0 | 14 | 1.0 | 14.0 |
| | | | 2.0 | 0.75 | 2.0 | 2.75 | 2.0 | 5.8 | | | | | 2.0 | 12.4 |

* The curves in figure 3 were made from these data. Ionization meters for measuring accurately grenz ray dosages are not available therefore the absorption data for grenz rays may have to be revised

Since our interest is mainly in the skin, we attempted to show to what degree radiation of 10 to 140 kilovolts peak are absorbed in successive millimeters of skin. The absorption data in table 4 were plotted and superimposed on a cross-sectional diagram of the skin with correct dimensions. Figure 5 shows the actual depth doses (read as horizontal distances) of the various radiations. It is therefore a chart directing the selection of qualities of radiation adequate for effective doses at various depths and for the treatment of lesions at such

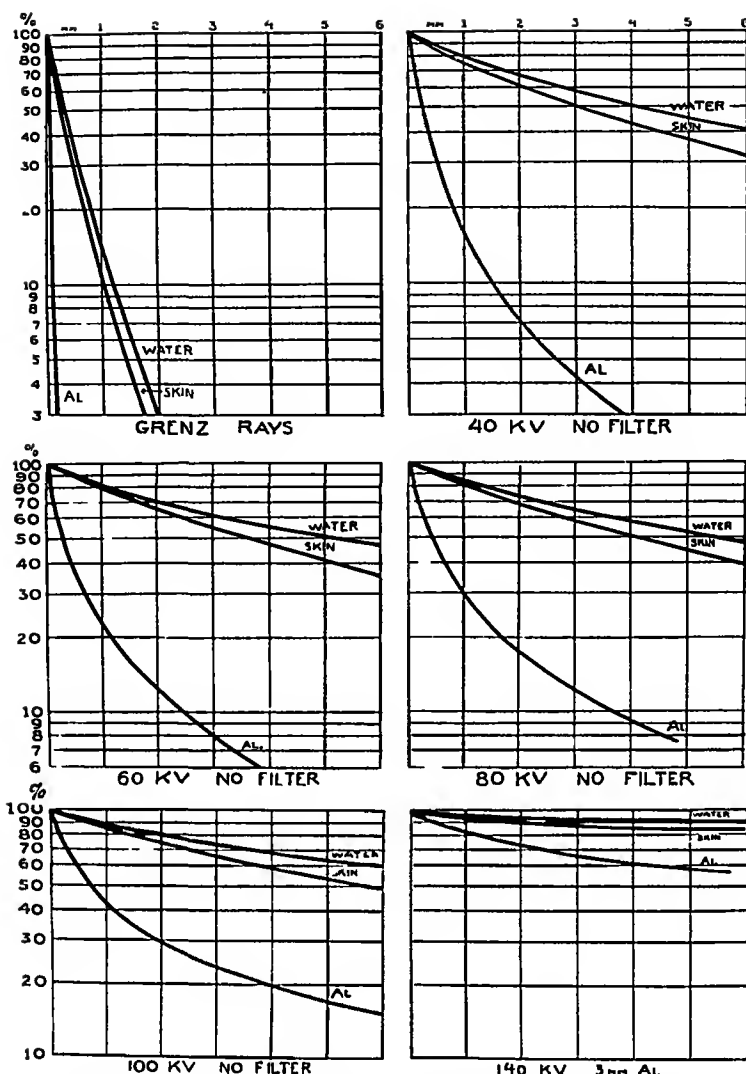


Fig 3—Semilogarithmic absorption curves for human skin, water and aluminum with radiations commonly used in dermatology

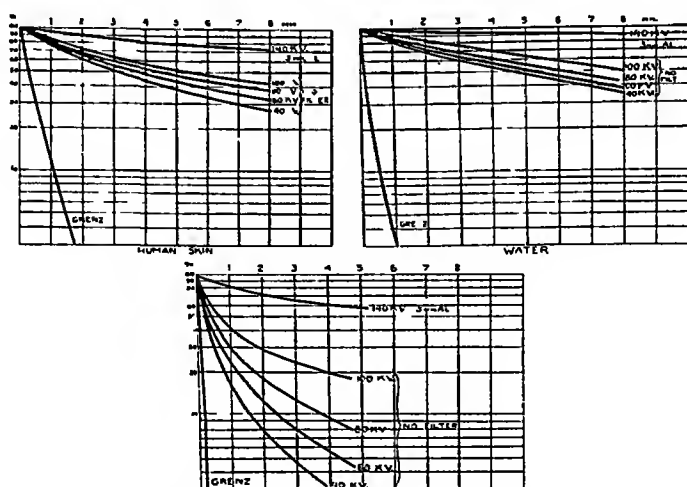


Fig 4—Semilogarithmic absorption curves for human skin, water and aluminum with varying voltages. These curves show the relative thicknesses of the different test materials required to absorb a given percentage of radiation

depths The diagram illustrates several interesting points which we wish to emphasize They are

1 Grenz rays are absorbed except for about 15 per cent of the intensity in the first millimeter of skin

2 Radiations of 40 to 100 kilovolts peak show differences of absorption of only about 16 per cent at a depth of 6 mm, at a depth of 3 mm the difference is only about 10 per cent This tends to show that for dermatologic roentgenotherapy with nonfiltered radiation rays the lower voltages (40 kilovolts) should be practically as effective as the higher (100 kilovolts)

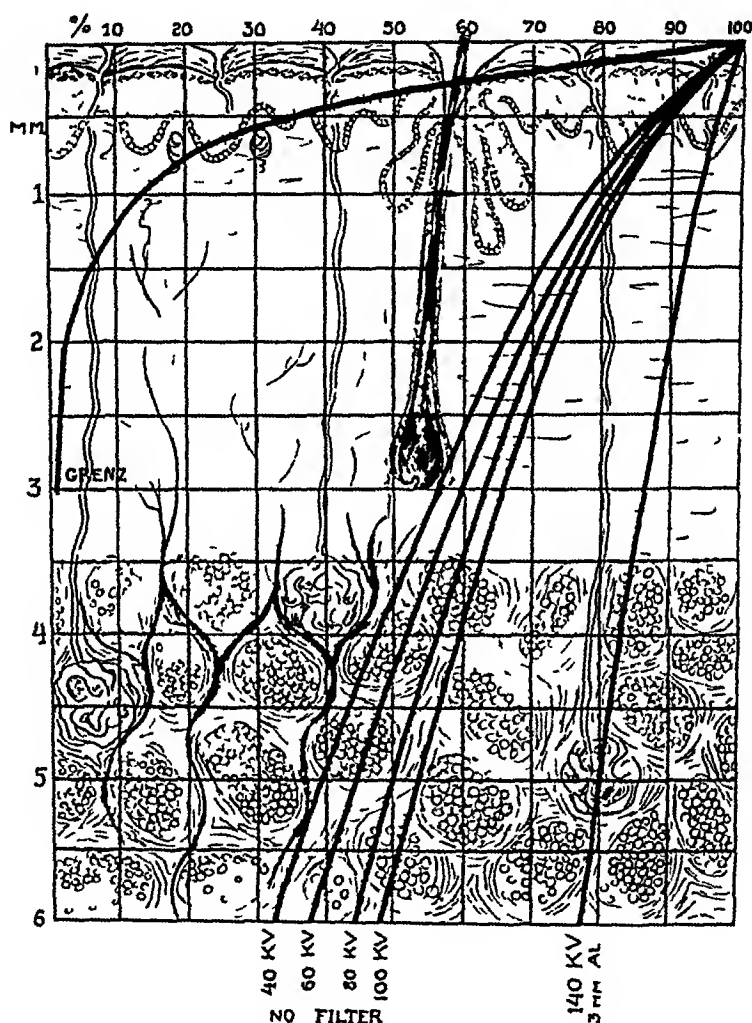


Fig 5—Absorption curves showing depth doses of various radiations used in dermatologic practice superimposed with correct dimensions over a cross-sectional diagram of the skin

3 Filtered high voltage radiations (137 kilovolts peak and a 3 mm aluminum filter) are very penetrating At the 3 mm level there is an absorption of 13 per cent of the incident beam, and at a depth of 6 mm the absorption is only 22 per cent

4 The half value layer in skin for varying voltages may be read directly from the diagram Thus, for grenz rays it is 0.35 mm, for 40 kilovolts it is 3.7 mm, for 60 kilovolts it is 4.2 mm, for 80 kilovolts it is 5.0 mm, for 100 kilovolts it is 5.57 mm and for 137 kilovolts with a 3 mm aluminum filter it is 20.5 mm

COMMENT

The measurement of depth doses has interested radiotherapeutists for many years. Isodose charts are available for treating lesions at any depth. These, however, are of little value to dermatologists because they deal with large thicknesses of tissues. Meyer's¹ article contains interesting and valuable charts dealing with depth doses and qualities of radiation. The data presented by Andrews and Braestrup² were based on experiments performed with photographic film. Our work was done with an ionization meter of the thimble type which was standardized in terms of readings of a standard chamber.

Roentgen doses expressed in international roentgens give little information regarding the biologic reaction. All reactions to the roentgen rays are atomic reactions and consist in the change of a neutral atom into an ion. As a result, chemical reactions take place in the cell, which produce biologic changes. The extent of the biologic changes depends not only on the duration of the irradiation and on the intensity of radiation which reaches the lesion but also on that portion of the radiation which is absorbed in the unit volume of the lesion. There is a definite difference in cutaneous reactions with different qualities of radiation. There have been many articles written to show this difference, including the two by MacKee and Cipollaro.³ The effect of radiation is influenced by its quality. The number of roentgens applied to the surface is no indication of what goes on deep in the tissues. Filtered high voltage radiation produces biologic reactions quite different from those produced with unfiltered low voltage radiation even though the surface effect, that is, the erythema or the effect on a few layers of cells (*Drosophila* eggs), may appear to be the same. In spite of these differences, it is advisable for practical therapeutic purposes to express physical measurements in terms of biologic reactions.

CONCLUSIONS

1 For small areas and for small thicknesses of animal skin (1 to 4 mm) the freely circulating blood does not increase or decrease absorption of the roentgen rays to any appreciable extent.

2 For superficial irradiation of human skin, the data obtained with dead tissue can be applied to living tissue.

1 Meyer, W. H. The Co-Relation of Physical and Clinical Data in Radiation Therapy, *Radiology* **32** 23 (Jan.) 1939.

2 Andrews, G. C., and Braestrup, C. B. Measurements of the Depth Dose for Roentgen Therapy Used in Dermatologic Practice, *Arch. Dermat. & Syph.* **33** 446 (March) 1936.

3 MacKee, G. M., and Cipollaro, A. C. The Roentgen Unit in Dermatology, *Arch. Dermat. & Syph.* **30** 761 (Dec.) 1934, Roentgen Dosage in Dermatology Expressed in International Roentgens, *ibid.*, this issue, p. 1.

3 Freezing of dead human skin with solid carbon dioxide does not alter absorption when low voltage radiation is used

4 Absorption data obtained with water are directly applicable to live human skin

5 Curves representing absorption with radiations of 40 to 100 kilovolts peak show slight differences up to a depth of 2 mm. It can be assumed, therefore, that lesions situated at this level can be equally affected by a quality of radiation between 40 and 100 kilovolts peak

6 Grenz rays are sufficiently penetrating to be of some value in the treatment of lesions situated within the first 0.5 mm of skin. Lesions over 1 mm in thickness are not effectively influenced by grenz rays

7 Filtered roentgen rays (137 kilovolts with a filter of 3 mm of aluminum) are much more penetrating than unfiltered rays and deliver large doses to lesions at considerably greater depths

40 East Sixty-First Street

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ABSTRACT OF DISCUSSION

DR DONALD M. PILLSBURY, Philadelphia. Much credit is due Dr. Cipollaro and Dr. Mutscheller for this presentation, because although dermatologists employ roentgen rays extensively in therapy, they have not, with a few notable exceptions, contributed as much to the experimental aspect of roentgen therapy as have the radiologists. Certain considerations arise in one's mind in attempting to apply Dr. Cipollaro and Dr. Mutscheller's interesting findings to clinical practice. These become the more important if one approaches a more truly superficial type of roentgen therapy. First, I should like to ask whether any evidence exists concerning varying absorption by the different layers of the skin of roentgen rays of the relatively long wavelength used in these experiments. This might be particularly important in treating conditions in which the stratum corneum is thickened and in which a major portion of the radiation might be absorbed in a region which is physiologically inactive. Second, the inherent filtration of the particular tube which is being used must be considered. Tubes vary greatly in this regard, and it must be kept in mind that even though the same kilovoltage is used roentgen rays of rather different quality may be emitted from different tubes. With a tube with a low inherent filtration, the proportion of rays of long wavelengths would be higher and the effects might even be more superficial than Dr. Cipollaro and Dr. Mutscheller obtained with the tube used in their experiments. It seems to me that this is a matter of great practical significance.

DR GEORGE C. ANDREWS, New York. I was particularly interested in hearing this paper because it is along the same lines as one I read two or three years ago on the measurement of the depth dose of roentgen rays in millimeters below the surface of the skin (Andrews, G. C., and Braestrup, C. B. *ARCH. DERMAT. & SYPH.* 33:446 [March] 1936). For our experiment, Dr. Braestrup and I used tissue fresh from the operating room and animal tissue. We found that we were unable to overcome loss of moisture, which made that method inaccurate. Because the tissue dried up, we gave up the use of tissue and found

the photographic film method best. We also thought that the inclined filter method we described was more reliable and accurate than the use of an absorption chamber. For the frame filter method with a water phantom, the filter is arranged at an inclined angle in a water bath and irradiation applied over that, the effect is measured at 1, 2 and 3 mm up to 15 mm depth. Our measurements by this method when rechecked were more satisfactory than when we used tissue. Dr Cipollaro and Dr Mutscheller tried to avoid back scattering in their measurements. There are some good reasons for doing that. The definition of a roentgen does not include back scattering. But in dealing with skin, we always have back scattering in the tissues which are exposed. Our method included back scattering. The condition is therefore as it actually is in the skin. I think that further work along these lines is desirable.

DR GEORGE M. MACKEE, New York. I wish it were possible to discuss in this connection the advantages and disadvantages of filtered radiation as compared with what is generally called unfiltered irradiation. In the future all radiation used by dermatologists will be filtered, although it will probably be called unfiltered. Shock-proof apparatus is undoubtedly the equipment of the future. Filtration with such apparatus is roughly the equivalent of 0.5 mm of aluminum. Dr Pillsbury mentioned an important fact, namely, that the inherent radiation is filtered by the glass wall of the tube. In the past there was considerable variation in the thickness of the wall and therefore in the filtration. For this reason the output varied over 50 per cent. Some of the old tubes caused as much filtration as does the shock-proof apparatus. Modern tubes do not vary in wall thickness. What Dr Cipollaro and Dr Mutscheller have attempted to do was to determine absorption in millimeters and loss of tissue more accurately than has heretofore been possible. In this work I was much surprised, as was pointed out, at the slight difference in absorption at 40 kilovolts and 60 kilovolts. It is proper to criticize this article on the basis of possible error. I do not know what the experimental error may be, but I believe it to be slight. Dr Cipollaro has consulted physicists, physiologists and biochemists in an effort to make the work as accurate as possible, and all said that it is as accurate as it can be at present. I think that it is sufficiently accurate for practical purposes. From this work a little more is learned about the selection of the quality of radiation in so far as it can be selected for lesions at various thicknesses and various depths.

DR EARL D. OSBORNE, Buffalo. I gathered from the charts that there was considerable difference in the amount of absorption between 60 or 70 kilovolts and 100 kilovolts. I should like to ask as a matter of practical treatment whether Dr Cipollaro feels that it is desirable for a dermatologist treating lesions not deeper than 2 or 3 mm to use 100 kilovolts rather than 60 to 70 kilovolts. In my personal experience I have a feeling that 70 kilovolts for practical purposes in treating cutaneous conditions is a maximum that one need not exceed, and my results at least seem better with 70 kilovolts than with a higher dose, and there is less danger of deeper effects. I use shock-proof apparatus and have had the manufacturer grind down the windows so that they are equivalent to 0.5 mm of aluminum. There was an inherent filtration of 12 mm of aluminum in the tube as it came out.

DR ANTHONY CIPOLLARO, New York. Dr Pillsbury asked whether there is a difference in absorption in the different layers of the skin. Yes, there is. We determined this experimentally and found that the epidermis, cutis and subcutaneous tissues absorbed varying percentages of the incident beam. The fat absorbed less

radiation than the skin. Absorption curves obtained with epidermis, cutis and fat were compared with those obtained through rabbit skin, rabbit ear and water. It was found that rabbit skin absorbed more radiation than human skin. The inherent filtration of the glass wall of the tube cannot be eliminated. A Coolidge tube was used in our experiments. My understanding is that at present the thickness of the glass wall of all modern Coolidge tubes is about the same. With modern shock-proof apparatus used for superficial therapy, there is an inherent filtration equivalent to approximately 0.5 mm of aluminum.

Dr Andrews brought up the question of loss of moisture from operating room specimens which were used in our experiments. We avoided this loss in two ways: first, by doing experiments on the same day that the human skin was obtained and, secondly, by putting the specimens in a Ball jar which contained a piece of moist gauze and was tightly closed. This prevented evaporation. Therefore, the specimens of human skin which we used had suffered no loss of water.

Dr Andrews and Dr Braestrup performed similar experiments several years ago, but they measured differences in intensity with photographic film. The obvious objections to this method were enumerated in my discussion of their paper. In our experimental work we avoided back scattering because we were interested only in the absorption of an incident x-ray beam without the effect of scattering. Therefore, in the absorption experiments through water our special device permitted us to measure the transmission of an x-ray beam through a column of water of varying thicknesses. The figures that we obtained measured the quantity of the x-ray beam which was transmitted without the effects of back scattering.

Dr MacKee spoke about filtration. Our absorption curves show that for ordinary superficial lesions filtration is not necessary. Lesions up to 5 mm in thickness should theoretically respond to treatment with roentgen rays of 40 as well as 100 kilovolts. We shall conduct carefully controlled clinical experiments with these lower voltages and shall report our results in a future communication.

DISEASES OF THE NAILS

REPORT OF CASES OF ONYCHOLYSIS

EVERETT C FOX, M D
DALLAS, TEXAS

There is considerable evidence that diseases of the nails, excluding the pyogenic and fungous infections and changes associated with the inflammatory dermatoses, are often produced by endocrine dysfunction, particularly hypothyroidism and hypopituitarism. There is a definite relation between some dermatologic conditions and the endocrine glands. The influence of the hormones on development and function of the skin, hair and nails is well established. In the past five years I have observed more than 30 cases of spontaneous separation of the nails, in a large portion of which there were symptoms indicative of hypothyroidism and a lowered basal metabolic rate. The majority of the patients have improved on medication with thyroid. In a few cases relapse has occurred with the development of new separations of the nails after thyroid medication was discontinued.

Diseases of the nails are many times overlooked, and careful attention to the nails will often be found a valuable aid to both the dermatologist and the general practitioner in the diagnosis of systemic diseases. Some indication of the frequency of ungual involvement may be obtained from reports such as that of White,¹ who observed 485 cases of diseases of the nails. Pardo-Castello² observed 464 patients, 192 (41.37 per cent) of whom had abnormal nails. The nails were affected by the same conditions that attack the general surface of the skin. Many cutaneous diseases produce ungual symptoms. General systemic diseases, such as the anemias, avitaminosis and the endocrine disturbances, may present important changes of the nails.

White¹ in his report of 485 cases of diseases of the nails found that 141 patients had onycholysis. The condition in 24 of these was associated with eczema, in 15 with trauma, in 21 with paronychia, in 37 with psoriasis, in 11 with syphilis and in 11 with fungous

From the Department of Dermatology and Syphilology, Baylor University, College of Medicine

Read at the Sixty-Second Annual Meeting of the American Dermatological Association, Inc., Monte-Bello, Quebec, Canada, June 1, 1939

1 White, C J. Clinical Study of Four Hundred and Eighty-Five Cases of Nail Diseases, Boston M & S J 147 537 (Nov) 1902

2 Pardo-Castello, V. Diseases of the Nails, South M J 27 377 (May) 1934

diseases. However, he apparently did not limit his cases to those of spontaneous separation of the nail from its bed.

The term onycholysis should be used in a more restricted sense, designating only spontaneous separation. The progress of the disease is usually gradual, beginning at the lateral free border of the nail and gradually increasing, with separation of the nail from the nail bed and the development of a space which may at times be filled with debris. The separation may be slight, but it frequently increases until the anterior half or two thirds of the nail is raised from the nail bed and occasionally until the nail is separated from its attachment at the matrix and is easily removed or shed. The surface of the nail is smooth, and there is no inflammatory process of the paronychium. The entire process is painless, and the separation remains over a long period, or there is improvement and regression. At times the nails become entirely normal, and after weeks or months recurrence takes place. There are fewer case reports of onycholysis in the literature than of almost any other condition of the nails.

Pardo-Castello³ reported cases of onycholysis from syphilis, eczema, psoriasis and anemia and others in which the cause could not be ascertained. Strauss⁴ reported 1 case of onycholysis and 1 of onychomadesis. Chargin⁵ reported a case of typical onycholysis "idiopathica" which developed during pregnancy and increased after term. He described the typical separation beginning at the free margin and gradually increasing until a third or more of the nail was involved. Templeton⁶ has reported 5 cases of separation of the nails of young women as an industrial disease related to the washing of paste from bottles. Viecelli⁷ observed the condition in a tanner who soaked his hands in brine. Heller⁸ examined 562 patients with endocrine disturbances and found only 8 instances of ungual disease of glandular origin. In his monograph⁹ he described 10 cases of onycholysis of indefinite causation and stated that in the literature there are reports of 40 or 50 cases of endocrine disturbances with pathologic changes of the nails, in 16 of

³ Pardo-Castello, V. Diseases of the Nails, Springfield, Ill., Charles C. Thomas, Publisher, 1936, p. 142.

⁴ Strauss, M. J. Onycholysis and Onychomadesis, Arch. Dermat. & Syph. **26**: 644 (Oct.) 1932.

⁵ Chargin, L. Onycholysis Idiopathica, Arch. Dermat. & Syph. **21**: 1051 (June) 1930.

⁶ Templeton, H. J. Onycholysis, J. A. M. A. **97**: 1950 (Dec. 26) 1931.

⁷ Viecelli, J. D. Onycholysis, Arch. Dermat. & Syph. **33**: 697 (April) 1936.

⁸ Heller, J. Onychopathologie und Endokrinologie (nach Beobachtung an 562 Fällen endokriner Störungen), Deutsche med. Wchnschr. **52**: 786 (May) 1926.

⁹ Heller, J. Die Krankheiten der Nägel. Berlin: Julius Springer, 1927, pp. 113 and 308.

which there was some type of dysfunction of the thyroid. The nails were described as atrophic, dystrophic, hypertrophic, dry, fragile, lusterless, thickened, irregular, slow growing and opaque.

This report is based on the study of 30 cases of abnormality of the nails, some of which were not followed sufficiently to give accurate final observations. Of the 30 patients, 28 were women and 2 were men. Twenty-seven had multiple separations, and 3 had separation of a single nail. Twenty had low basal metabolic rates, and 15 of these had other symptoms suggesting hypothyroidism, such as a tendency to gain weight easily, a requirement of eight to ten hours' sleep, easy fatigability, exces-

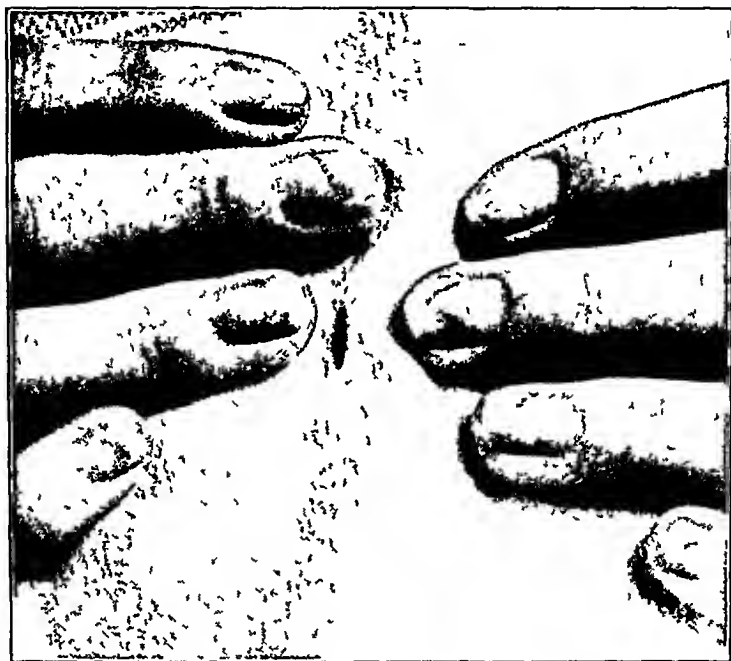


Fig 1 (case 5) —Separation of all the nails of both hands except that of the left index finger. The basal metabolic rate was -13 per cent. The nails became normal after thyroid medication.

sive susceptibility to cold weather, dryness of the skin and hair and brittle nails. Several had what I termed winter pruritus (*pruritus hiemalis*), with dryness of the skin over the entire body and in cool weather annoying itching, which was aggravated by frequent bathing. The skin usually assumed a normal appearance in warmer weather. One patient had psoriasis of the elbows, but there was no evidence of psoriasis of the nails, another had lichen planus without any inflammatory process of the nails, and 1 had recovered from lichen planus several months previously. Twenty-one showed improvement on thyroid medication, 3 did not improve and 3 were not observed for a sufficient period to

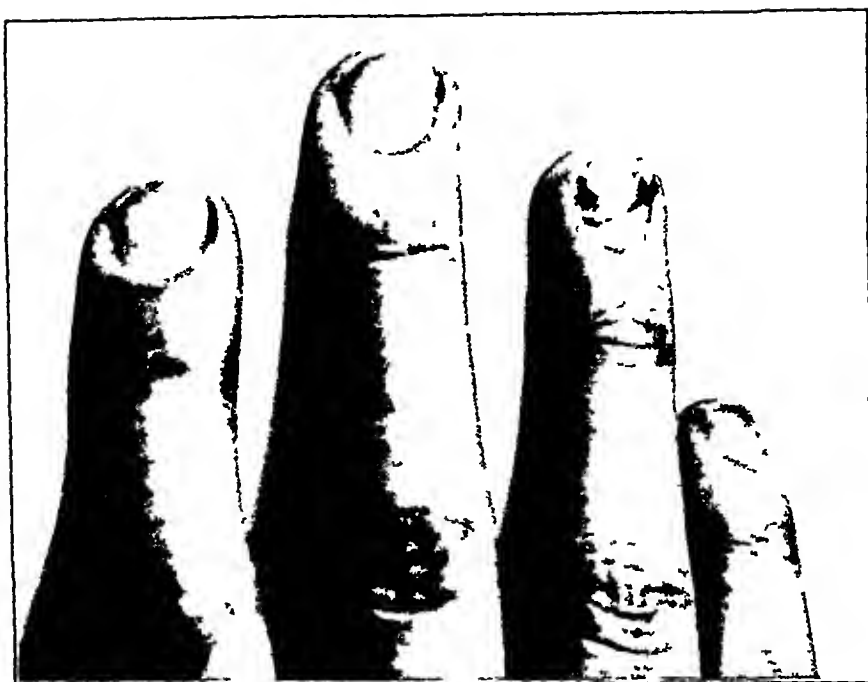


Fig 2 (case 3) —Separation of the nail of the right ring finger. The nail was removed surgically, but separation developed after regrowth. The separation improved and recurred. After thyroid medication the separation disappeared, and the nail has remained normal.

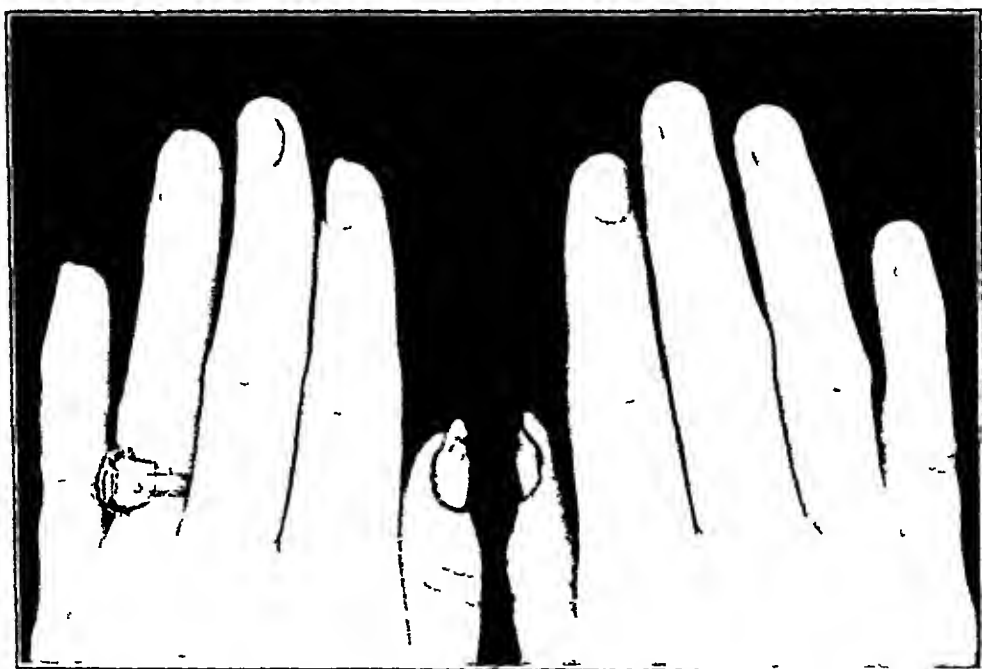


Fig 3 (case 11) —Symptoms suggesting mild hypothyroidism. The basal metabolic rate was $+11$ per cent. The nails were entirely normal at the end of five months with 2 grams (0.13 Gm) of thyroid extract daily.

determine the final results. The separation developed in 1 case while the patient was taking 10 grains (0.65 Gm.) of thyroid daily, and the basal metabolic rate was found to be +15 per cent. The nails improved rapidly when thyroid was discontinued. One patient had had symptoms suggesting hyperthyroidism ten years previously and improved with iodine medication, but at the time of the nail separation the basal metabolic rate was -12 per cent and there were definite symptoms of hypothyroidism. Two patients had multiple separations from chemical irritation. In 3 patients an unexplainable factor was observed, in 1 case by Shelmire¹⁰ and in 2 by me, in which there was a definite history of acute exacerbation of the nail separation, evidenced by tenderness and a 1 to 2 mm. horizontal erythematous inflammatory band

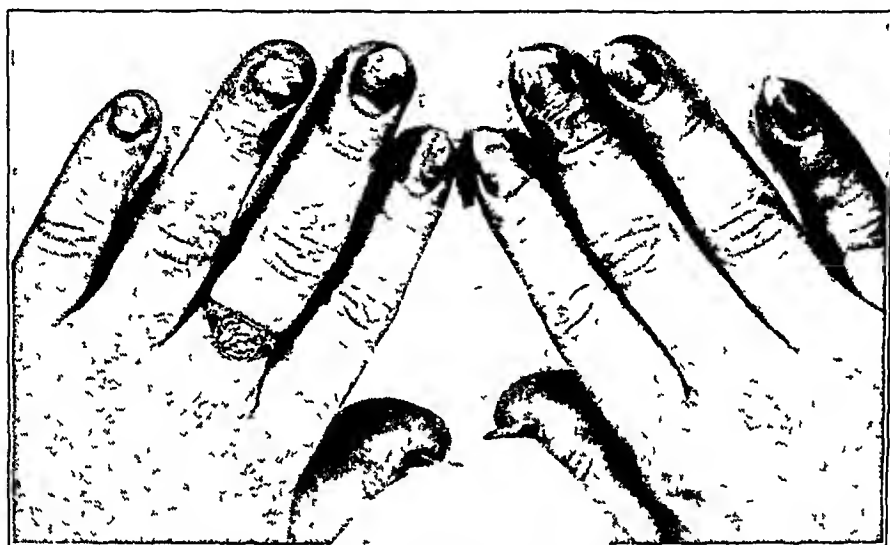


Fig 4 (case 30)—Eczematoid dermatitis of terminal phalanx of each finger with extensive nail separations produced by irritation from permanent waving fluid

adjacent to the line of separation, which developed within twenty-four hours and lasted one or two days after the ingestion of alcohol.

Marie and Woringer¹¹ reported a case of koilonychia associated with acrocyanosis and hyperhidrosis. Mixed glandular therapy resulted in the development of normal nails. Wander¹² observed a girl aged 9 years with dry, brittle nails, scanty hair, hyperkeratoses of the fingers and toes and painful palmar hyperkeratoses. The nails were thickened

10 Shelmire, B. Personal communication to the author.

11 Marie, G., and Woringer, F. Un cas de koilonychie. Guérison après traitement par un extrait pluin glandulaire, *Bull. Soc. franç. de dermat. et syph.* **37** 1214 (Dec.) 1930.

12 Wander, W. G. Dystrophy of the Finger Nails and Toe Nails (Spoon-Nails), *Arch. Dermat. & Syph.* **27** 1011 (June) 1933.

Data on Thirty Cases of Abnormal Nails

| Case | Patient | | | Associated Symptoms | Involvement of Nails | Basal Metabolic Rate | Comment |
|------|---------|-----|-----|---|--|----------------------|--|
| | Race | Sex | Age | | | | |
| 1 | W | I | 35 | Gains weight easily | Separation of nails of right middle finger and left ring, middle and little fingers | -12 | Gradual improvement from 2 grains (0.13 Gm) thyroid daily entirely normal nails at end of 5 months |
| 2 | W | F | 55 | Dry skin, freezes, sleeps excessively, tires easily, psoriasis of elbows, no pitting nails | Separation of nails of right ring and little fingers and left little finger, aggravated by ingestion of alcohol | -16 | From 2 grains (0.13 Gm) thyroid daily improved gradually, but condition recurred when thyroid was discontinued during influenza, nails became normal when thyroid was resumed patient became pregnant |
| 3 | W | F | 32 | Separation of nail, removed surgically but recurred, improved and recurred for 2 years | Separation of nail of right ring finger, recurred 3 months after surgical removal | -26 | Improved gradually from 2 grains (0.13 Gm) thyroid daily later B M R -2 and nails better than for last 3 years remained normal |
| | | | | | | -21 | |
| 4 | W | I | 24 | Gains weight, freezes, dry skin, sleeps 10 hours | All nails partially separated for 6 months, right index and left middle fingers show 75% separation | -12 | Improving from 2 grains (0.13 Gm) thyroid daily two nails removed surgically and regrew normally, 1 year required for all nails to become normal |
| 5 | W | I | 25 | Sleeps 10 hours, gains weight, tires easily, hands cold and moist | Separation of nails of right thumb, index, middle, ring and little fingers and of all left fingers except index | -13 | 2 grains (0.13 Gm) thyroid daily, nails became normal |
| 6 | W | I | 20 | Freezes in winter, gains weight easily, skin dry | Separation of several nails | -4 | Improved rapidly from 1 grain (0.06 Gm) thyroid daily no recurrence in 2 years |
| 7 | W | I | 41 | Dry skin, hair and nails, gains weight easily, susceptible to cold, sleeps 8 to 10 hours | For 4 years has had recurrent separations of nails right thumb nail became complete and was shed 4 years ago improved from thyroid $\frac{1}{2}$ grain (0.05 Gm) daily, separations recur when thyroid is discontinued | -5 (4 yrs ago) | For several years has improved from small dose thyroid recent B M R -4 started $1\frac{1}{2}$ grains (0.09 Gm) thyroid daily, with rapid improvement, condition recurred when thyroid was discontinued |
| 8 | W | I | 72 | Freezing in winter, skin, hair and nails dry, gains weight, palms dry, mildly keratotic 10 years ago very nervous with rapid pulse took iodine with rapid improvement | Nails began to separate 2 years ago and have improved and become worse, right little finger, 90% separation, right middle finger, 75%, right ring finger, 25%, right index finger thickened and dystrophic | -12 | Started with $\frac{1}{2}$ grain (0.03 Gm) thyroid daily and in 3 weeks gradually increased to 2 grains (0.13 Gm) daily nails improved rapidly stopped thyroid because of nervousness separations recurred |
| 9 | W | I | 33 | Skin dry in winter sleeps 8 to 10 hours | All nails dry and brittle more marked last year with longitudinal striations has had recurrent separation for 5 years (right little, ring and index fingers and left little ring and index fingers) | -18 | Thyroid gradually increased to 2 grains (0.13 Gm) daily with improvement of nails after 1 month, which continued nails normal at end of 2 months |

Data on Thirty Cases of Abnormal Nails—Continued

| Case | Patient | | | Associated Symptoms | Involvement of Nails | Basal Metabolic Rate | Comment |
|------|---------|-----|-----|---|---|----------------------|---|
| | Race | Sex | Age | | | | |
| 10 | W | F | 35 | Menstrual irregularity for several years, roentgen sterilization | Separation of all nails on right hand and of left thumb, ring and middle finger nails, toe nails also separated | —11 | Improved from thyroid and recurred with influenza, fair results on 2 grains (0.13 Gm) daily but recur from time to time probably hypopituitary also |
| 11 | W | F | 24 | Freezes, dry skin, excessive sleep, overweight | Separation of nails of right middle and index fingers and thumb and of left middle and index fingers and thumb | +11 | 2 grains (0.13 Gm) thyroid daily, nails were improved in 2 months and normal at the end of 5 months |
| 12 | W | F | 33 | Symptoms suggest mild hypothyroidism | Separation of nails of right ring and little fingers and of left little finger | None | Improved with thyroid at end of 2 months unable to obtain further observation |
| 13 | W | F | 49 | Blood pressure 180/120 to 240/150 for 3 to 4 years, sleeps 9 hours, gains weight, freezes in winter, 7 miscarriages, had 6 roentgen treatments to nails, no improvement | Separation of nails of right index, middle and ring fingers, left thumb and middle and ring fingers | —25 | Nails improved slowly, blood pressure dropped to 150/90 lower than in years, 2 grains (0.13 Gm) thyroid daily B M R now —8 nails improve and recur and recently on 1 grain (0.06 Gm) thyroid, but not a satisfactory result |
| 14 | W | M | 45 | No history suggestive of thyroid deficiency | Separation of nails of right middle, ring and little fingers, half separation of all nails on left, nails dark, with some dystrophic changes | —15 | Unable to follow results |
| 15 | W | M | 31 | Nails separated 5 years ago and have improved and become worse, mother, 70, has same condition | Separation of all nails on right and of nails of left thumb and index, middle and ring fingers | —5 | Slight improvement on high vitamin diet for 1 year and then recurred 2 grains (0.13 Gm) thyroid daily produced rapid improvement in 6 weeks then sudden recurrence followed by improvement |
| 16 | W | F | 34 | Drowsy, lethargic, gains weight easily taking thyroid 3 years for B M R —35 recent excessive menses | Separation of nails of right little and ring fingers, left little and ring fingers, separation increased by alcohol 10 grains (0.65 Gm) thyroid daily now | +15 | Thyroid stopped, nails rapidly improved, patient feels much better |
| 17 | W | F | 36 | Has had separation of nails for 4 months B M R low 3 years ago thyroid taken for some time | Separation of all finger nails and great toe nails | Low 3 yrs ago | Unable to follow |
| 18 | W | F | 41 | Menses irregular, freezes skin dry large doses of arsenic for last year for leichen planus no evidence of leichen planus of nails | Multiple separation of slight degree | —9 | Improved with thyroid ½ grain (0.03 Gm) daily and were normal in 4 months |
| 19 | W | F | 52 | Leichen planus for 6 months, no inflammatory lesions of nails | Slight separation of several nails at lateral distal edge | —1 | Improved rapidly with thyroid, ½ grain (0.03 Gm) daily recurrence 1 year later improved rapidly again on ½ grain (0.03 Gm) thyroid daily thyroid continued, nails remained normal |

Data on Thirty Cases of Abnormal Nails—Continued

| Case | Patient | | | Associated Symptoms | Involvement of Nails | Basal Metabolic Rate | Comment |
|------|---------|-----|-----|---|---|----------------------|---|
| | Race | Sex | Age | | | | |
| 20 | W | F | 49 | Freezes, dry skin, B M R —15 3 years ago, took thyroid for a time | Separation multiple 1 year ago improved with roentgen therapy, recent recurrence of nail separations | —6 | Improved with roentgen therapy and recurred, now taking 2 grains (0.13 Gm) thyroid daily and improving slowly |
| 21 | W | F | 44 | Gains weight, sleeps 9 hours, nervous, married 22 years, no pregnaneles | Separation of right ring and index fingers for 1 year, index nail removed surgically | —27 | Improved slowly with thyroid and ovarian extract, nail removed regrew normally after starting thyroid and other nail became normal in 1 year |
| 22 | W | F | 37 | Dry skin gains weight, freezes, B M R —24, 1 to 5 grains (0.32 Gm) thyroid for 1 year but none the last year | Dry, brittle fingernails, two nails separated slightly | —17 | Started thyroid with improvement of general symptoms, nails improved rapidly |
| 23 | W | F | 25 | Nails dry and brittle with white spots | Separation of nails of right index and left middle fingers, nails dry, brittle and pitted, with white spots | —10 | ½ grain (0.03 Gm) thyroid daily for 1 week, stopped because of nervousness nails improved with roentgen therapy |
| 24 | W | F | 22 | Sleeps 9 to 10 hours, dry skin, freezes in winter, irregular menses | All nails show early separation with 2 mm red band at point of separation about distal edge | —8 | Unable to get subsequent observation |
| 25 | O | F | 39 | Separation and dystrophy of nails | Separation of nails of right middle and index fingers and thumb, left middle finger and thumb | —15 | 2 grains (0.13 Gm) thyroid daily improved right index and thumb nails removed surgically and regrew normally, separation of others gradually returned to normal |
| 26 | W | F | 46 | Fracture of terminal phalanx, freezes, gains weight sleeps 9 hours, tires easily, previous B M R, —23 | Separation of nail after fracture of finger | —19 | 2 grains (0.13 Gm) thyroid daily and roentgen therapy, improved recurred with typhoid fever, became normal on continued thyroid medication in 6 months |
| 27 | W | F | 37 | Freezes, sleeps excessively, easily fatigued | Onychia, irregular, thickened, dark buckled nails, early separation of nail of right index finger | —27 | 1½ grains (0.13 Gm) thyroid daily for 5 months nails normal no recurrence in 2 years |
| 28 | W | F | 34 | Skin and hair dry freezes, sleeps 8 to 9 hours repeated miscarriages | Separation of finger and toe nails and other dystrophic changes for 4 years eversion of nails of each little finger space filled with hyperkeratotic material | —19 | Fair improvement of separation no change in dystrophies, has had recurrent separations multiglandular dysfunction |
| 29 | W | F | 24 | Mild eczematoid dermatitis about finger tips | Nails of right thumb and index and middle fingers separated from formaldehyde solution (beauty parlor) | None | Dermatitis disappeared and nails improved on avoiding formaldehyde solution |
| 30 | W | F | 21 | Edema and eczematoid dermatitis of terminal phalanx of each finger fingers remain moist with permanent wave fluid | All nails of both hands show ¼ to ½ separation | None | Wet dressing and ammoniated mercury ointment produced rapid improvement condition recurs when same wave fluid is used |

and dark, the teeth separated and the gums spongy. The basal metabolic rate was — 47 per cent. She showed rapid improvement by prolonged treatment with thyroid extract.

Duemling¹³ observed a white man aged 23 who had marked thickening of the palms and soles, general loss of hair and a basal metabolic rate of — 13 per cent. He was otherwise well developed and in good health. His nails were ragged and split and covered only about half the nail bed. Duemling considered the changes typical of those noted in children with myxedema and cretinism and considered the case one of hypothyroidism. Barney¹⁴ reported a case in which one toe nail became white and separated from the nail bed, when the nail regrew it was thick and yellowish. Later all nails of the fingers and toes became involved and were elevated from the nail bed, thin and brittle, the nail plates were uneven and showed longitudinal striation. The toe nails were thickened and elevated, and the space beneath was filled with horny masses. The Wassermann reaction was negative, scrapings and cultures for fungi gave negative results, the values for blood calcium and phosphorus were normal, the basal metabolic rate was — 15 per cent. No improvement was noted from a high vitamin diet or from administration of thyroid.

Barrett,¹⁵ in his report on the hereditary occurrence of hypothyroidism with dystrophic changes of the nails, presented the case of a patient with disorders of the hair and nails and abnormalities of the mental and nervous system. The scalp hair was scant and the eyebrows and the axillary and pubic hair reduced. The nails were short of the finger tips, the edges were thick and broken, with absence of the lunula. Histologic examination of the skin showed a myxedematous condition. The patient improved when given 5 grains (0.32 Gm.) of thyroid three times daily. The nails continued to grow, there was an increase of perspiration and an increased growth of hair of the scalp and eyebrows, and the exfoliation of the hands improved. The study of this patient's family of 61 members in six generations revealed that 14 of them had had abnormal changes of the nails and hair and varying types of mental change. Tobias¹⁶ reported a similar case in which there was dystrophy of the nails and changes of the hair, and in the patient's family of 25

13 Duemling, W. W. Dystrophy of the Hair and Nails, Keratoderma of the Palms and Soles, Hypothyroidism, *Arch. Dermat. & Syph.* **29** 163 (Jan.) 1934.

14 Barney, R. E. Dystrophy of Nails, *Arch. Dermat. & Syph.* **31** 721 (May) 1935.

15 Barrett, A. M. Hereditary Occurrence of Hypothyroidism with Dystrophies of the Nails, *Arch. Neurol. & Psychiat.* **2** 628 (Dec.) 1919.

16 Tobias, N. Hereditary Familial Dystrophy of the Nails, *J. A. M. A.* **84** 1568 (May 23) 1925.

persons covering four generations there were 12 with such dystrophic changes. Jacobsen¹⁷ studied a family consisting of 64 members in five generations, 22 of whom had dystrophic changes in the nails and 18 of whom were hairless or had only scant downy hair. He stated that the cause was uncertain, but that certain of the physical changes in these persons are also seen in persons suffering from endocrine deficiency, notably hypothyroidism, and he concluded that there was considerable evidence to suggest that hypothyroidism may be directly inherited. Thompson¹⁸ studied a similar family, of 65 members in four generations, 16 of whom had dystrophic changes of the nails, 11 were men and 5 were women. Some showed improvement when roentgen therapy was given, and they were later treated with thyroid medication. No report of follow-up observations was made.

Alderson¹⁹ observed a white woman aged 49 with severe onychauxis involving all the finger nails and to less extent the toe nails. She improved rapidly on administration of thyroid, $\frac{1}{2}$ grain (0.03 Gm.) three times daily for two weeks and then 1 grain (0.06 Gm.) three times daily for several months. The nails were considered normal at the end of nine months.

Behn and Besancon²⁰ reported the case of a boy aged 13 whose finger and toe nails became rough, thin and friable and who had a basal metabolic rate of —17 per cent.

Rostenberg²¹ presented a woman aged 37 who for ten years had abnormal nails, there were atrophic and dystrophic changes which involved more than a third of the nail. The nails were roughened, pitted and discolored. The Wassermann reaction was negative, the basal metabolic rate was +48 per cent on one occasion and later was +22 per cent. A similar case in which there was associated hyperthyroidism, was described by Heller⁹ in his monograph. Pardo-Castello³ observed 2 cases of atrophy of finger and toe nails associated with hyperthyroidism. Shelmire¹⁰ observed a patient with severe exophthalmic goiter who had separation of all the nails. Two months after partial thyroidectomy the nails were normal. Surgeons observing

17 Jacobsen, A. W. Hereditary Dystrophy of the Hair and Nails, *J. A. M. A.* 90:686 (March 3) 1928.

18 Thompson, H. B. Hereditary Dystrophy of the Nails, *J. A. M. A.* 91:1547 (Nov. 17) 1928.

19 Alderson, H. E. Onychauxis and Thyroid Therapy. *Arch. Dermat. & Syph.* 5:602 (May) 1922.

20 Behn, C. W., and Besancon, J. H. Dystrophy of the Nails, *Arch. Dermat. & Syph.* 27:359 (Feb.) 1933.

21 Rostenberg, A. Anonychia and Onychatrophia Acquisita, *Arch. Dermat. & Syph.* 26:581 (Sept.) 1932.

a large number of cases of hyperthyroidism say that they frequently see separation of the nails and consider this condition one of the symptoms of hyperthyroidism

In an analysis of 150 cases of myxedema, Hun and Prudden²² found changes of the nails in 75 per cent. Howard found abnormal nails in 86 per cent and changes in the hair in 93 per cent of his patients with myxedema

Hollander and Fisher²³ observed a patient whose finger and toe nails were opaque, with dark brown discolored areas. The lunulae were absent, and the case was considered one of hypopituitarism. Guy, in discussing the case, stated that he had observed a similar condition due to hypothyroidism

Hollander²⁴ reported a case of onychauxis due to hypopituitarism. The patient was a white boy aged 9 years who had dry, rough, brownish, grooved and transversely striated nails of both the hands and the feet. Dryness of the skin and hair had developed gradually, with absence of axillary and pubic hair, small genitalia and feminine characteristics. Hollander also described 2 cases of dystrophia adiposogenitalis²⁵ with changes of the hair and nails, small genitalia and obesity. He considered the cutaneous and ungual changes a result of the glandular dysfunction.

Combes²⁶ observed a boy aged 12 years who presented dystrophic changes of the nails and keratoses of the palms associated with Frohlich's syndrome. The nails were hypertrophic, opaque, ridged and brittle. The toe nails were similar and presented severe onychogryposis. The basal metabolic rate was — 21 per cent.

Lisser²⁷ observed a eunuchoid who had suffered a testicular injury eleven years previously. The nails of the fingers and toes were dry, brittle and increased in thickness. Implantation of testicular substance produced great general improvement, and the nails became normal. Lisser stated that trophic disturbances of the skin, hair, nails and teeth are common in deficiency diseases of the glands of internal secretion, particularly hypothyroidism, hypopituitarism and hypogonadism.

22 Hun, H, and Prudden, T. M. Myxedema, *Am J M Sc* **96** 1 (July) 1888, cited by Barrett¹⁵

23 Hollander, L., and Fisher, J. W. Onychauxis, *Arch Dermat & Syph* **30** 453 (Sept.) 1934

24 Hollander, L. Onychauxis Due to Hypopituitarism, *Arch Dermat & Syph* **2** 35 (July) 1920

25 Hollander, L. Pituitary Gland Dystrophies, *Arch Dermat & Syph* **7** 632 (May) 1923

26 Combes, F. C. Onychauxis and Keratosis Palmaris, *Arch Dermat & Syph* **24** 711 (Oct.) 1931

27 Lisser, H. Onychauxis in a Eunuchoid, *Arch Dermat & Syph* **10** 180 (Aug.) 1924

Pende²⁸ observed fragile, thin nails with striae, white spots, atrophy and slow growth with similar changes of the hair in hypoplastic conditions, particularly hypothyroidism. In hypopituitarism the lunula is small or absent. Hypogonadism produces thin nails. In hyperthyroidism and hyperpituitarism there are well developed, shiny nails that grow rapidly. Meakins²⁹ stated the belief that low metabolism is observed in diseases due to deficient function of the pituitary, adrenal and gonad glands without symptoms of myxedema. The adrenal gland raises metabolism through the effect of epinephrine on cells and by its influence on the thyroid.

White³⁰ has reported 7 cases of changes in the nails which were considered due to avitaminosis, in 2 of these cases there were lowered basal metabolic rates. They did not improve on administration of thyroid, but high doses of vitamins B₂ and D produced rapid improvement. Pardo-Castello³ stated that he has seen no cases of changes in the nails proved due to vitamins. Clinical experimentation³¹ seems to indicate that the administration of vitamin A by mouth may produce cutaneous effects similar to those sometimes seen after administration of thyroid preparations. This is seen especially in cases of "dry skin," brittleness of the nails and follicular keratoses and in some cases of keratotic palms and soles and in mild ichthyosis and erythroderma. Goldsmith³² in a discussion of vitamins stated that vitamins A and B₁ are antagonistic to thyroxin, vitamin C deficiencies cause a diminished production of epinephrine while vitamin D is synergistic with parathyroid, especially in tetany. Vitamins may have an indirect endocrine effect or function³³.

Anderson³⁴ recently reported a case of spoon nails, dysphagia and cheilitis in a woman suffering from severe anemia. In his conclusion he stated that the ungual changes were possibly due to mild hypothyroidism which is frequently associated with severe anemia.

28 Pende, N. Constitutional Inadequacies. An Introduction to the Study of Abnormal Constitutions translated by S. Naccarati, Philadelphia, Lea & Febiger, 1928, p. 140.

29 Meakins, J. C. The Practice of Medicine, ed 2, St. Louis, C. V. Mosby Company, 1938, p. 883.

30 White, C. Onychia Due to Chronic Hypovitaminosis. J. A. M. A. **102**:2178 (June 30) 1934.

31 Wise, F., and Sulzberger, M. B. The Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers Inc., 1938, p. 6.

32 Goldsmith, W. N. Recent Advances in Dermatology, Philadelphia, P. Blakiston - Son & Co., 1936, p. 485.

33 Cowgill, G. R. The Vitamin B Requirements of Man, New Haven, Conn., Yale University Press, 1934.

34 Anderson, N. P. Syndrome of Spoon Nails, Anemia, Cheilitis and Dysphagia. Arch. Dermat. & Syph. **37**:816 (May) 1938.

CONCLUSIONS

1 Cases of onycholysis associated with reduction in the basal metabolic rate are reported. Improvement followed thyroid medication in the majority of the cases.

2 Considerable evidence is presented that there is a relation between diseases of the nails and endocrine dysfunctions.

3 The influence of the hormones on the development of the skin* and its appendages in both physiologic and pathologic processes should receive more consideration from the dermatologist.

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ABSTRACT OF DISCUSSION

DR V PARDO-CASTELLO, Habana, Cuba. Dr Fox has done well in calling attention to the cause of these dystrophies of the nails. He has been unusually fortunate to gather such a large number of cases of onycholysis and to prove in the majority of them an etiologic connection with hypothyroidism, as shown by the low basal metabolic rate and by the excellent results of the specific treatment.

However, onycholysis is not always due to hypothyroidism. I believe that it may be due to a host of different causes among which thyroid dysfunction seems to be a frequent one.

I agree with Dr Fox that aside from the infectious, traumatic, parasitic and symptomatic diseases of the nails coincident with diverse dermatoses, the conditions of the nails produced by endocrine disturbances are the most common. This report shows how a disturbance of the nail growth may be the first, and for the time being the only, apparent symptom of endocrine imbalance. I think that physicians in general do not pay enough attention to the minor changes of the nails, which may yet be of importance in arriving at a satisfactory diagnosis in many cutaneous, as well as other, diseases.

DR J GARDNER HOPKINS, New York. I am grateful to Dr Fox for this presentation because some light on disorders of the nails is certainly needed. I should like to ask Dr Fox whether he has seen any spoon nails. I have seen several cases in which the patient had the same type of basal metabolic rate he reports in the low range of normal and in which the condition of the nails improved after medication with thyroid extract. Another point of great interest to me is that the table of basal metabolic rates, if I made it correctly, shows many rates from — 12 to — 14. Such rates are usually regarded as normal. I am sure, however, that in certain cutaneous diseases rates in the lower range of normal have to be regarded as significant.

DR SAMUEL AYRES JR, Los Angeles. I should like to ask Dr Fox if he made any observations on the condition of the toe nails of these patients in correlation with the finger nails. I thought possibly that there might be some significance in the fact that so many of these patients are females. That also calls up the question of nail polish and polish removers containing acetone and other ingredients having affected the nail. I have encountered many women showing separation of the nails or transverse splitting, which I have always regarded as possibly due to nail polish or polish remover. I wonder whether the separation from the nail bed in some of Dr Fox's cases might not be of the same nature.

DR S WILLIAM BECKFR, Chicago. Dr Fox asked me to discuss this paper, since I have made a study, as yet unpublished, of certain diseases of the nails which included a rather large percentage of cases of onycholysis. The study was inspired

by a patient with severe onychia of the type called by Heller "onychogryphosis due to eczema" and described in the *Archiv für Dermatologie und Syphilis* (163 337 1931). My patient was 30 years of age and had had the condition for eight months. All of the nails of the right hand and the first two of the left hand were involved in a severe overgrowth and were yellow and crumbly. In addition to the changes in the nails, the involved fingers of both hands showed chronic exudative dermatitis without definite vesiculation. Repeated search for fungi by both the potassium hydroxide method and culture was fruitless. Capillary studies of the folds of the nails which were yet uninvolved showed vasodilatation. The patient was presented before the Chicago Dermatological Society (*ARCH DERMAT & SYPH* 24 698 [Oct] 1931), where the consensus was in favor of a fungous origin. Further search was made by potassium hydroxide preparations and culture, with negative results. Portions of the nail were removed, sectioned and studied microscopically, but no fungi were found. When even a small amount of nail had been removed, pain was experienced and bleeding was evident. There was therefore extensive overgrowth of the nail bed itself. On section, blood vessels and collections of nucleated cells were seen, but no fungi.

Since fungi could not be found, it was decided to treat the patient as though only the dermatitis were present, which was diagnosed exudative neurodermatitis. The dermatitis cleared up immediately, and the nails became normal just as soon as new nails could grow. Some three years later juxta-articular nodules developed due to syphilis, which had been contracted in the meantime. The patient was again presented before the Chicago Dermatological Society (*ARCH DERMAT & SYPH* 31 744 [May] 1935), at which time the diagnosis was confirmed and the nails were normal.

In contrast to this severe type of onychia, other patients with exudative neurodermatitis show milder changes of the type usually called "eczema of the nails." Patients with the dry type of neurodermatitis (flexural, atopic eczema), on the other hand, show a type of onychia which falls in the classification of onycholysis, which is the subject of Dr. Fox's paper. I found that treatment of the neurodermatitis caused the lesions of the nail to improve, so that in case there is no mechanical reason for the onycholysis, as reported by Templeton, I make a diagnosis of neuro-onychial, treat the patient accordingly and obtain good results. I was much pleased to hear Dr. Fox link the changes in the nails with the disturbance of the endocrine system. I prefer to call the condition neuronychia, but, after all, I know that the sympathetic nervous system and the endocrine glands are inseparable functionally. Dr. Fox found onycholysis much more frequently in women. My studies have shown that functional disease is more frequent in women than in men, but not to so great a degree. The question of medication with thyroid has always intrigued me. When Dr. Russell Wilder of the Mayo Clinic was chairman of the department of medicine at the University of Chicago, I discussed with him the reason for the low basal metabolic rate in patients with functional disease. He did not know the exact cause but was inclined to doubt that it was due entirely to thyroid dysfunction. I have never tried medication with thyroid myself, but have had patients who had received it elsewhere, usually with disappointing results. It is gratifying to hear of Dr. Fox's excellent results. I should like to ask him whether capillary studies at the nail fold have been made in his cases, especially in normal nails, and whether any of his patients had other dermatoses.

DR HIRSH E. MUIFF, San Francisco. I should also like to ask Dr. Fox how he explains the high incidence of women—28 women to 2 men. It has occurred to me that while the basic cause may be metabolic the exciting factor probably is nail polish, acetone and similar preparations.

DR LOUIS A BRUNSTING, Rochester, Minn I should like to ask Dr Fox whether he has observed cases of frank myxedema in association with onycholysis. It should be recognized that reports of the basal metabolic rates, especially single readings, may be subject to a considerable percentage of error. Readings are of less importance generally in hypothyroidism than in hyperthyroidism. In cases of extensive involvement of the skin by exfoliative dermatitis, the basal metabolic rate is elevated often to 50 per cent above normal without evidence of hyperthyroidism. In these cases there is an alteration from normal in the radiation of body heat, and the basic formula for recording the rate by the measurement of the exchange of oxygen and carbon dioxide through the lungs does not obtain. The administration of thyroid extract in cases in which there is a lowered basal metabolic rate is usually well controlled, but a word of warning may be in order in the use of such treatment in the goiter belts and in the management particularly of older persons who may have an adenoma of the thyroid.

DR EVERETT C FOX, Dallas, Texas In answer to Dr Brunsting's question regarding the basal metabolic rates, I have found low basal metabolic rates in many of these patients, as noted in the table, but I have not found any patients with clinical myxedema. I believe that one can determine more from the clinical history and physical examination regarding thyroid deficiency than by the basal metabolic rate, particularly as it is usually done, by the patient's going to the laboratory on the morning of the test. It is more accurate when the patient is hospitalized over night, and some patients have shown lower rates when checked that way. The dose of thyroid extract has been kept low because of what Dr Brunsting mentioned. In no case has the dose been raised above 3 grains (0.195 Gm.) daily. When I have to give more than that, the patient is turned over to an internist or an endocrinologist. Regarding nail polish, most of my patients have been told at the beauty parlor that this is the cause of their trouble and as a result have left off nail polish for months. This factor certainly has to be considered as well as other irritants. Disturbances of the nails from chemical irritants, such as a solution of formaldehyde and permanent wave fluid, were reported in beauty parlor operators. Several patients had involvement of the toe nails, but certainly not as frequently as of the finger nails. I do not know why the series should be as high in women except for the explanation offered by Dr Becker of nervous and vascular instability. I think that in some of these cases there is probably more chance for vascular disturbance than in others. Certainly a low basal metabolic rate may be observed in many of them. In some cases dyshidrosis has been classified as a neurovascular disturbance, and low basal metabolic rates have been present. Capillary studies have not been made. Many of the patients would probably have capillary changes associated with the changes of metabolism and the growth and cornification of the nails. There are a number of reports in the literature on spoon nails, some of which have improved on medication with thyroid. In many cases the condition of the nails has been associated with anemia. Almost invariably, severe anemia is associated with hypothyroidism. The changes in the nails probably occur as a result of hypothyroidism associated with severe anemia. I appreciated Dr Pardo-Castello's discussion. Certainly this method of treatment will not cure onycholysis in all cases. Hypothyroidism is only one etiologic factor of a large group which includes pyogenic and fungous infections and changes associated with the inflammatory dermatoses as well as endocrine dysfunctions. The condition may also be related to trauma. In this particular group that I am reporting, I believe that under the method of treatment used the patients have shown more improvement and have remained well longer than those treated by any other means previously used.

URINARY EXCRETION OF INDOXYL (AS INDICAN) BY INFANTS WITH ECZEMA

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Interest in the metabolism of a compound essentially toxic and regularly formed in the enteric canal will continue, at least until a complete clarification of the mode of its detoxication is established. Furthermore, the toxicity of the compound will continue to justify studies directed toward disclosing the relation between it and disease processes. I have reference to the substance indole. This heterocyclic nitrogenous compound, a degradation product of the amino acid tryptophan, has as yet achieved no clinical significance beyond its traditional indictment of complicity in the production of so-called autointoxication or biliousness. This relation has the laboratory background of an increased excretion of indican in the urine, determined by crude qualitative tests.

The introduction of newer and more accurate analytic methods in biochemistry not alone supplies instrumentalities for the elucidation of physiologic and clinical problems but serves as inspiration for the testing of theories in physiology and pathogenesis. Furthermore, the newer analytic methods in measurement of the indoxyl derivatives of indole have sponsored the continued interest in the metabolism of indole. My interest in the problem dates from my development of quantitative analytic methods for the estimation of indoxyl compounds in urine and blood.

By these methods the following data have been established (1) the normal concentration of indoxyl in blood,¹ (2) the daily excretion of it in urine² as indican in amounts far in excess (75 to 150 mg) of what had until then been considered within the normal range, and (lately) (3) the excretion in the newborn of indican in amounts com-

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1 Sharlit, H. A Method for the Quantitative Estimation of Indoxyl Compounds in Blood, *J Biol Chem* **104** 115, 1934, The Concentration of Indoxyl Compounds (Indican) in Blood, *J Lab & Clin Med* **20** 850, 1935

2 Sharlit, H. A Method for the Quantitative Estimation of Indoxyl Compounds in Urine, *J Biol Chem* **99** 537, 1933

parable in terms of relative body weight to that excreted by adults.³ It was this last finding that supplied the background for the study herein reported and the base line from which to interpret the findings.

The several features of indole metabolism definitely established are these:

1 Indole is wholly of exogenous origin (formed in the intestines from tryptophan).

2 One way of detoxicating it is through oxidation to indoxyl and conjugation with sulfuric acid to form indican (potassium indoxyl sulfate). This is accomplished by the liver.

3 Indican is harmless and readily excreted by the kidneys.

4 The administration of indole orally or parenterally⁴ increases indican excretion in an amount to account for but 50 per cent of the exhibited indole.

5 The route or routes of passage of the other 50 per cent of indole are still unknown, and the possibility that these routes represent failure to detoxicate effectively poses the danger of indole to the integral organism.

6 The excretion of large amounts of indican in the urine may be accepted as evidence of inordinate putrefaction of protein in the intestine.

Single chance samples of urine were collected from each of 35 infants between the ages approximately of 2 months and 2 years, each of whom had an eruption and most of whom had some form of eczema. The specific gravity of each sample (except a few in which the total volume was too small for an acceptable reading) was carefully taken and a quantitative determination made for indican. The specific gravity is a substantially adequate index of the concentration of the solids in urine and may properly serve to indicate, with respect to a given dissolved constituent, the importance of the general concentration of the dissolved solids in the sample examined. This rapid check on the significance of excretion in chance samples, when the chief concern is knowledge of the absolute amount excreted on a twenty-four hour basis, is the only one available when the collection of twenty-four hour excretions is well nigh impossible, as was the case with these nonhospitalized infants.

For this reason the results of the analyses given in the table are listed in an order determined by the specific gravity of the several

3 Sharlit, H. Indican Excretion in the New-Born, *Arch. Pediat.* 55:277, 1938.

4 Sharlit, H. Unpublished data. Similar findings have been published by others.

samples. Therein will be noted a definite correlation between indican concentration and specific gravity—evidence of the anticipated reliability of the specific gravity in marking the influence of the general density of the sample on the concentration of indican found. This was also found in the samples from healthy newborn infants, though with those the total nitrogen was used as an index to the measure of concentration of the solids. On the whole, it must be said that these data gave definite evidence of an indican excretion in these infants in excess of

Results of Analyses of Urine (Cases Listed in Order of Ascending Values of Specific Gravity of Samples Examined)

| Case No | Age | Diagnosis | Specific Gravity of Urine | Indican, Mg per Liter |
|---------|--------|-------------------------------|---------------------------|-----------------------|
| 1 | 2 yrs | Dermatitis venenata | 1.007 | Faint trace |
| 2 | 20 mos | Infantile eczema | 1.007 | Trace |
| 3 | 4 mos | Infantile eczema | 1.010 | Faint trace |
| 4 | 7 mos | Atopic eczema | 1.013 | Trace |
| 5 | 2 mos | Infantile eczema | 1.013 | 25 |
| 6 | 1 yr | Atopic eczema | 1.014 | 16 |
| 7 | 1 yr | Atopic eczema | 1.016 | Trace |
| 8 | 4 mos | Infantile eczema | 1.017 | Trace |
| 9 | 1 yr | Infantile eczema | 1.018 | Trace |
| 10 | 2 yrs | Infantile eczema | 1.018 | 47 |
| 11 | 17 mos | Atopic eczema | 1.019 | 40 |
| 12 | 2 yrs | Impetigo, dermatitis venenata | 1.020 | 17 |
| 13 | 2 yrs | Infantile eczema | 1.020 | 39 |
| 14 | 2 yrs | Urticaria | 1.021 | 27 |
| 15 | 14 mos | Infantile eczema | 1.024 | 32 |
| 16 | 2 yrs | Neurodermatitis | 1.024 | 18 |
| 17 | 5 mos | Infantile eczema | 1.025 | Trace |
| 18 | 2 yrs | Infantile eczema | 1.026 | 44 |
| 19 | 2 yrs | Infantile eczema | 1.026 | 30 |
| 20 | 2 mos | Infantile eczema | 1.026 | 29 |
| 21 | 2 yrs | Dermatitis venenata | 1.027 | 84 |
| 22 | 2 yrs | Pyoderma | 1.027 | 35 |
| 23 | 2 yrs | Urticaria | 1.028 | 47 |
| 24 | 2 yrs | Infantile eczema | 1.030 | 17 |
| 25 | 15 mos | Atopic eczema | 1.031 | 54 |
| 26 | 1 yr | Herpes simplex | 1.031 | 80 |
| 27 | 10 wks | Seborrheic eczema | 1.032 | 84 |
| 28 | 2½ yrs | Atopic eczema | 1.033 | 62 |
| 29 | 21 mos | Infantile eczema | 1.033 | 80 |
| 30 | 2 yrs | Infantile eczema | 1.034 | 67 |
| 31 | 1 yr | Atopic eczema | ? | Trace |
| 32 | 2 yrs | Infantile eczema | ? | 38 |
| 33 | 2 yrs | Neurodermatitis | ? | 78 |
| 34 | 2 yrs | Infantile eczema | ? | 87 |
| 35 | 16 mos | Infantile eczema | ? | 59 |

what might have been expected on a basis of my reported findings in the healthy newborn, though distinctly less than might have been anticipated in the presence of protein putrefaction.

To the extent that this is an exposure of the true state of affairs it may be concluded that eczema in infants is not usually associated with enteric protein putrefaction. I believe that conclusion to be in general harmony with clinical opinion and experience with eczema of infants; however, this statement must be read in the light of the influence of intestinal stasis and its definite relation to indican production.

Costiveness regularly increases indicanuria, and an intestinal purge may be relied on to reduce it precipitately. Constipation is a complaint so common that physicians have almost come to ignore it as a contributing factor to disability, yet those who make a fetish of combating it as the first approach in the relief of none too obviously explained symptoms have on countless occasions reported astonishing success. How important constipation is in the practice of dermatology is impossible to judge. Certainly reported studies pertaining thereto are exceedingly few. Still, constipation as a possible factor in the production or the maintenance of eczema in infants is seriously considered. Goodman and Burr⁵ in the histories of 206 cases of infantile eczema reported constipation present in 85 per cent. Strickler, Fisher and Lowenburg⁶ studied the gastrointestinal motility by roentgen examination of the tract in 33 children with the eczema of infants and found intestinal stasis in more than half of them. Of course, the pediatric approach to the therapy of eczema in infants regularly stresses the necessary attention to accompanying constipation or diarrhea. My data may be said to corroborate these reported findings of constipation in infants with eczema.

Sagers,⁷ of the medical corps of the United States Navy, recently made a short report in the service medical bulletin, which, strangely enough, he called "Allergy, Autointoxication and Indicanuria." In a group of service men with varying, etiologically elusive complaints (including 1 with eczema) he followed the plan of recording the degree of indicanuria in several samples from each patient each day and correlating these findings with the nature of the diet in terms of specific articles of food. By elimination and substitution of articles of diet, he sought for each patient a list of foodstuffs that led to a minimum indicanuria. On diets so determined his patients reported much relief. Incidentally, the patient with eczema was cured. I mention without comment his theory that irritation of the intestinal mucosa may influence the selective absorptions through that lining and admit to the circulation toxins and the elements necessary to invoke symptoms and, I presume, to assist in setting up the allergic mechanism.

My findings, too, may be said to support in a negative way the concept of an allergic background in most of these infants with eczema. While the production of indican is a hepatic function, too little is known

5 Goodman, H., and Burr, M. E. Eczema in Infancy and Childhood, *Arch Pediat* **54** 30, 1937.

6 Strickler, A., Fisher, M. K., and Lowenburg, H. A Probable Etiological Factor in Infantile Eczema Based on X-Ray Examinations of the Gastro-Intestinal Tract, *Arch Pediat* **53** 397, 1936.

7 Sagers, J. K. Allergy, Autointoxication and Indicanuria, *U. S. Nav. M. Bull.* **34** 67, 1936.

of the complete story of indole metabolism to justify a discussion of this function on the basis of only this type of investigation. Speaking generally of the problem of intestinal putrefaction, it may be pointed out that indican production may serve as a reliable measure of its existence as directly applicable to protein digestion. In this connection, attention may be called to the possible usefulness of this type of investigation as correlative to studies in porphyrin production. The seemingly confused findings resulting from the quantitative studies on porphyrin elaboration in cases of suspected photosensitive dermatoses may receive clarification if such studies receive accompanying estimations of indican production as a measure of the putrefactive background for the various porphyrin body formations.

To probe by sampling the probable fertility of a way of study in the elucidation of disease processes can never in itself give completely meaningful findings. When the attempt results in a dry bore, publication of the experiment seems justified only if the procedure per se has genuine physiologic meaning. For then publication calls attention to a helpful way of study of other and possibly more appropriate problems. I believe this to be true with respect to the study of indole metabolism.

One need make no plea in these times for routine urinalysis in dermatologic practice. Quantitative indican measurements can be routinely secured with ease, and it is not beyond expectation that through such routine recordings evidences or clues may be revealed when even ingenious casting here and there might fail to produce a "haul."

SUMMARY

The quantitative estimation of indican on chance samples of urine in 35 cases of infantile dermatoses, chiefly eczema, showed definitely increased excretions, probably due to intestinal stasis.

ABSTRACT OF DISCUSSION

DR MARION B SULZBERGER, New York. I am not competent to discuss Dr Sharlit and Dr Klumpp's paper from the chemical or the biochemical point of view, but I think one can take it for granted that they have demonstrated a quantitative difference between normal infants and infants with infantile eczema in regard to a certain component of the urine. They explain this difference on the basis of the probable existence of constipation in infants with eczema as contrasted to infants without eczema. In my material, most eczematous eruptions in infants are not seborrheic or contact type dermatitis but atopic dermatitis. There is now a rather long list of observations on the obvious alterations in atopic persons as contrasted to normal persons. For example, one can say that atopic persons are inclined to have vasomotor instability, including vagotonia, that many seem to have slightly more than the normal tolerance for sugar, that many have white dermographism, and now, perhaps, that they are inclined to spasm and to spastic constipation. The question is: What may one conclude from the finding of these abnormalities? At present, I believe one can conclude only that the abnormality

is, in all probability, related in some way to the atopic condition. It may be the result of the atopic constitution or the result of the presence of atopic disease—in this instance, a cutaneous manifestation of atopy. In other words, here the cutaneous disease may be in some way attributable to the constipation, or the constipation may be in some way due to the cutaneous disease or both may be the result of some third factor. It seems to me that it is today quite obvious that the existence of disease often depends on a chain of many links, and the breaking of only one of these links may be sufficient to interrupt the chain of factors operative in the causation of the disease. That explains why in some cases atopic disease may respond to combating of the constipation, in others to correcting the sugar tolerance, in others to sedatives, in others, to rest, to change of environment, to reducing the exposure to atopens, and in some even to relieving nervous tension or psychic stresses. It is probable that in each instance therapy has simply attacked one of the factors and has broken one link in the chain on which the existence of disease depended.

DR HERMAN SHARLIT, New York. I think there is a practical implication in the use of estimations of indican in the control of constipation. Many disease processes are complicated by it. The fact that one knows about a physiologic factor (constipation) which never operates in favor of the patient but usually against him is good reason to feel that it is good practice to attempt to clear it up. In dealing with eczema or atopic dermatitis, one is invariably impressed with the idea that diet may have something to do with it. In approaching this dietary phase, rather than attempt elimination and substitution of special foodstuffs helter skelter, one would do better to direct such changes under the guidance of a test on urine, such as for indican. Aiming to bring indicanuria to a minimum may be an effective approach to the dietary phase of the treatment of eczema. The technic of estimation may be readily adapted to office practice.

Clinical Notes

GENERALIZED EXFOLIATIVE PSORIASIS AND MYCOSIS FUNGOIDES

IRVING L. SCHONBERG, M D, CLEVELAND

Keil,¹ in an extensive study of parapsoriasis en plaques disséminées and incipient mycosis fungoides, suggested that the former dermatosis probably is the precursor of the latter in most, if not all, cases. Wise and Sulzberger,² commenting on this observation, stated the belief that the incidence of mycosis fungoides would be much greater in a given community if this were true. They have, however, observed some cases of parapsoriasis en plaques in which there finally appeared, after years, clinical as well as microscopic evidence of mycosis fungoides. Fox,³ in 1913 reported a case of mycosis fungoides following psoriasis.

The case to be described here is deemed worthy of report since long-standing psoriasis was followed by mycosis fungoides.

REPORT OF A CASE

Past History—J. S., a Jew 45 years of age, had, except for a dermatosis, enjoyed good health. The eruption started thirty-four years before I saw him, as "red spots" over his entire body. These spots soon acquired a scaly character and finally coalesced, forming large scaly red plaques. During the past year he had noticed red rings and patches which appeared different from the original lesions. During the past thirty years he had noticed improvement during the warm weather, but during the last summer the areas had seemed more persistent. Until the last year there had been no subjective symptoms. During the past few months itching had been a notable feature, especially over the chest and abdomen.

Present Illness—When first observed, on Feb. 13, 1939, the patient presented a diffuse erythematous squamous process involving the scalp, face, trunk and extremities. On the scalp there was a "piling up" of silvery scales. The ears and upper eyelids and brows shared in the erythematous scaly process. On the trunk there were large areas, varying in size from that of a silver dollar to that of a palm, noninfiltrated, red, sharply demarcated and covered with loosely adherent scales. There were similar but smaller areas on the extremities. In addition to the scaly lesions, the trunk, back and thighs presented red and brownish red nummular plaques varying in size from that of a quarter to that of a palm,

1 Keil, H. Parapsoriasis en Plaques Disséminées and Incipient Mycosis Fungoides. A Critical Review with a Report of an Illustrative Case, *Arch Dermat & Syph* 37:465 (March) 1938, Parapsoriasis en Plaques Disséminées and Incipient Mycosis Fungoides. Supplementary Data on Their Relationship, *ibid* 38:545 (Oct) 1938.

2 Wise, F., and Sulzberger, M. B. Year Book of Dermatology and Syphilology for 1938, Chicago, The Year Book Publishers, Inc., 1938.

3 Fox, H. Mycosis Fungoides Following Psoriasis, *J. A. M. A.* 61:330 (Aug. 2) 1913.

definitely infiltrated and unquestionably distinct from the surrounding scaly skin. The borders were sharply defined and appeared to be slightly raised. Some of the lesions were annular in appearance. The ringlike infiltrations enclosed small scaly islands. The skin markings on the infiltrated areas were exaggerated. There were numerous crusted linear areas on the trunk and shoulders. On the lower extremities were several lima-bean-sized ulcerated areas accompanying varicose eczema.

The results of serologic examination of the blood and the blood count were normal. Histologic examination (by Drs. David L. Satenstein and Wilburt Sachs) was made of a section from a lesion on the chest.

Microscopic Description—Throughout the entire upper and middle portions of the cutis was an intense cellular infiltrate. It was composed of small round wandering connective tissue cells, plasma cells and histiocytes. Throughout this infiltrate in some areas a fine reticulum was present. There were some breaking up of the cellular elements and some grouping of the cells. In the upper part of the cutis there was a moderate amount of edema and leukocytes. The epidermis was irregularly acanthotic and in some small areas parakeratotic. In the other zones the granular layer was retarded. No cell nests were present in the epidermis. The microscopic diagnosis was mycosis fungoides.

SUMMARY

A case of mycosis fungoides is presented. This condition followed a long-standing generalized psoriasis, of thirty-four years' duration. Pruritus, which was absent for thirty-four years, developed after the appearance of the infiltrated plaques of mycosis fungoides.

524 Keith Building

HISTOLOGIC STUDY OF THE FREI REACTION PAPULE

LESLIE M. SMITH, M.D., EL PASO, TEXAS

The indolent character and the unusual persistence of the Frei test papule prompted its microscopic study at several stages of its evolution. Three patients with proved lymphogranuloma venereum were given injections of 0.1 cc of Frei antigen intracutaneously in the arm. Positive reactions developed in all, and no reactions were obtained in other persons who were used as controls. A papule was removed from one patient at the end of twenty-four hours, from another at seventy-two hours and from a third five days after the test was performed. These specimens were prepared according to routine and stained with hematoxylin and eosin.

APPEARANCE AT VARIOUS STAGES

Reaction at Twenty-Four Hour Stage—The epidermis showed marked intercellular and intracellular edema. Many of the cells were vacuolated, and in places there was some spongiosis, approaching vesicle formation. In the cutis there was moderate edema, and accumulations of lymphocytes and a few polymorphonuclear leukocytes were seen in perivascular spaces in the upper and middle strata.

Reaction at Seventy-Two Hour Stage—There were slight hyperkeratosis and some edema in the epidermis, though less edema than at the twenty-four hour stage. In the cutis light edema and a noticeable increase in connective tissue cells were apparent. In the perivascular spaces throughout the cutis and about the sebaceous and sweat glands there was a decided infiltration composed of lymphocytes. One sebaceous gland showed degenerative changes apparently due to the pressure of the infiltrate.

Reaction at Five Day Stage—The appearance differed little from that at the seventy-two hour stage. The epidermis showed less edema and no spongiosis. The infiltrate in the cutis was composed of lymphocytes which were massed about the vessels and superficial and deep parts of the appendages. Connective tissue cells were rather markedly increased.

COMMENT

The histologic picture of the Frei reaction is, then, as follows. Soon after the injection there is edema in the epidermis, with the production of spongiosis and histologic vesicles. It is easy to see how such a reaction might proceed to the formation of a clinical vesicle. After seventy-two hours this superficial edematous process subsides, and the cellular infiltrate in the cutis becomes more marked and is grouped around the blood vessels and appendages. Whereas early in the process the infiltrate is composed of lymphocytes and polymorphonuclear leukocytes, in the later stages it becomes practically a pure lymphocytic infiltrate with a decided increase in connective tissue cells. The rather dense character of the cellular infiltrate, extending fairly deep into the cutis, and the increase in connective tissue cells would seem to explain the indurated character and the persistence of the papule.

SUMMARY

A histologic study of Frei reaction papules at three stages of their evolution is presented, with the idea of correlating the clinical appearance of the papule and its histologic structure.

931 First National Bank Building

Minor Notes

SENSITIVITY TO GENTIAN VIOLET (METHYLROSANILINE)

MARVIN B GOLDSTEIN, M D , YOUNGSTOWN, OHIO

Mrs L W , a white woman aged 45, was first seen in September 1939, complaining of severe pruritus vulvae. A diagnosis was made clinically and microscopically of monilial infection. A 3 per cent aqueous solution of gentian violet (methylrosaniline) was prescribed. The monilial infection began to clear up, but wherever the solution came in contact with the skin pustular dermatitis developed. At one time a drop was spilled on the thigh, and the dermatitis developed on the site. A patch test was done on the arm, with a positive result. The patient was presented at the Pittsburgh Dermatological Society¹ while the dermatitis was still present.

The application of gentian violet was discontinued, and the dermatitis cleared up. Then the remaining monilial infection was treated with a 3 per cent solution of cresyl violet, with good results. The patient showed no sensitivity to the cresyl violet.

1 Goldstein, M B Arch Dermat & Syph, to be published

Obituaries

JOSEPH LEE KIRBY-SMITH, M D

1882-1939

Joseph Lee Kirby-Smith, a pioneer dermatologist in the South, was born in Sewanee, Tenn., in 1882. He was educated at the Sewanee Military Academy and at the University of the South Medical Department, graduating in 1906 from the latter institution with a degree of Doctor of Medicine and with highest honors. From 1906 to 1910 he did graduate work in dermatology in New York, including practice in services at Bellevue Hospital and at the New York City Department of Health hospitals, and served for eighteen months as a member of the house staff of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He also served as instructor of dermatology at New York University, at the Bellevue Hospital Clinic and at Dr. Fordyce's clinic.

He entered the practice of dermatology in Jacksonville, Fla., in 1911 and was active in practice until his death. For many years he served as chief of the department of dermatology at St. Vincent's, St. Luke's and Duval County hospitals and was dermatologist to the Riverside Hospital.

The Section on Dermatology and Syphilology of the Southern Medical Association, the Southeastern Dermatological Association and the Florida Society of Dermatology and Syphilology, of all of which he was a member, owe much to his genius for organization. He was also a diplomate of the American Board of Dermatology and Syphilology, a member of the American Medical Association, the American Society of Tropical Medicine and the American Society of Parasitology and a fellow of the American Academy of Dermatology and Syphilology.

He was born of fighting stock. His father was the confederate general Edmund Kirby-Smith, commander of the department of the Southwest during the Civil War. Though handicapped by deafness as a result of an accident while playing football, Dr. Kirby-Smith, like his illustrious father, never surrendered or asked quarter because of the odds against him but used his sharpened powers of observation and his keen analytic mind to nullify a physical handicap. Because of this handicap, it was in a clinic that Kirby-Smith was at his best, his remarks being always pointed and without equivocation.

He was remarkably resourceful and dextrous in cutaneous therapeutics, and his sincere and abiding interest in the welfare of his patients engendered their faith and confidence in him. With his striking, aggressive, jovial personality, he seemed tireless and for many years conducted one of the largest dermatologic practices in the country.

Kirby-Smith contributed numerous articles to the literature but is best known for his studies on *Agamemonatodum migrans* as a cause

of "creeping eruption" This work gained recognition abroad, and he discussed the subject before the London Medical Association in 1936 He was later awarded the degree of Doctor of Science by his Alma Mater for his research

His social activities included membership in the Phi Delta Theta fraternity, Florida Yacht Club and Sons of the American Revolution



JOSEPH LEE KIRBY-SMITH, M D
1882-1939

He was a member of the Church of the Good Shepherd During the World War he served as a First Lieutenant in the Medical Corps, and after the war he was appointed a consultant in the United States Public Health Service

Dr Kirby-Smith died in Jacksonville on Nov 5, 1939, after an illness of several months He is survived by a widow and three daughters

ELMO D FRENCH, M D

Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

ECZEMA AND ITS PRACTICAL MANAGEMENT F WISE and J WOLF, J A M A 111:2106 (Dec. 3) 1938

Wise and Wolf enumerate the factors thought to be primarily and secondarily responsible for eczematous eruptions. They do not believe that eczema in all instances is based on allergy. The mechanism of sensitization is unknown. Autosensitization has been proved by observation of the development of eczema after contact with serum from other eczematous patches. Wise and Wolf believe that mutation may occur from eczema to one of a group of diseases, such as dermatitis exfoliativa, mycosis fungoides, Hodgkin's disease and leukemia. While hypersensitivity may usually be acquired, they believe that there is often an inborn predisposition. Bacterial and mycotic infections appear to predispose to eczema, but Wise and Wolf doubt that the traditionally listed causes, such as alcoholism, digestive disturbances and endocrine disorders, have been proved to be of any special etiologic significance. Atopic dermatitis should be clearly differentiated from ordinary eczema. The authors list a detailed formulary for the topical and general treatment of patients with eczema.

COMBINATION COURSES OF BISMUTH ADMINISTRATION T SOLLMANN, H N COLE and K. HENDERSON, J A M A 111:2175 (Dec 10) 1938

Sollmann, Cole and Henderson and their collaborators advocate the use of combined bismuth preparations in order to keep the concentration of bismuth elevated. At first both a series of injections of a soluble bismuth compound and injections of an insoluble bismuth preparation are given. After two weeks the latter only is continued. This form of treatment is advocated in the treatment of patients with acute syphilis who are sensitive to arsenic, but it may be used also in the treatment of early syphilis.

SENSITIZATION REACTION TO SULFANILAMIDE E B ROGERS, J A M A 111:2290 (Dec 17) 1938

Rogers reports the case of a woman aged 58 who had previously had several local allergic reactions to injections of procaine, tutocain and butyn. After a recurrent attack of erysipelas, sulfanilamide therapy was instituted. Twenty-five grains (1.6 Gm) of the drug was taken orally in thirty-six hours. This was followed by swelling and redness of the eyelids, lacrimation and associated pruritus. An area of swelling and erythema was noted in the left groin. Similar lesions appeared at every site of previous application of a local anesthetic. After five weeks the condition had ameliorated. Rogers noted that sulfanilamide and the local anesthetics previously used all had a similar base, aminobenzene (aniline). A drug taken by mouth thus produced flare-up reactions at the sites of injections made years before.

ALLERGY IN CHILDHOOD III ITS ONSET AND NATURAL PROGRESS B RATNER, J A M A 111:2345 (Dec 24) 1938

According to Ratner, eczema is the prevailing allergic syndrome in infants under 1 year of age. Food sensitivities were demonstrated in every child who was tested, but further study demonstrated that the predominant allergen in 59

per cent of cases was an "environment contact" Sensitization in utero may not be uncommon Ratner avers that the onset of allergy may in a measure be prevented through control of the diet of the pregnant woman and of the young infant

ACTUAL SITE IN SKIN OF INTRADERMAL INJECTION F W TAYLOR, J A M A **111** 2475 (Dec 31) 1938

Taylor enlisted the help of several colleagues, and the skin of various animals as well as human skin was used as the site of intradermal injections of india ink Sections of the typical bleb produced in every case revealed the ink to be entirely in various depths of the corium This work indicates that an injected fluid is seldom inoculated into the epidermis even when an intradermal (extremely superficial) injection is given

PROGNOSIS OF SYPHILIS H J MORGAN, J A M A **112** 311 (Jan 28) 1939

In patients with asymptomatic syphilis the incidence of cardiovascular lesions and of involvement of the central nervous system is greater than in patients who react at the time of infection with acute lesions of the skin and mucous membranes The threat of untreated syphilis is great The earlier the infection the greater the menace to exposed persons Among women with untreated syphilis in pregnancy a healthy baby may be expected 1 time in 6 Infected infants commonly die The Negro male is vulnerable to cardiovascular lesions and the white male to neurosyphilis Acute syphilis is curable in from 90 to 100 per cent of patients From 70 to 80 per cent of patients with early latent syphilis need never suffer from any sequelae of the disease In cases of late latent syphilis treatment decreases the incidence of damaging lesions

THE TREATMENT OF VENEREAL LYMPHOGRANULOMA WITH SULFANILAMIDE A A KNIGHT and V C DAVID, J A M A **112** 527 (Feb) 1939

Knight and David report the cases of 2 patients with active lesions of venereal lymphogranuloma which had proved refractory to various methods of therapy In both cases, a favorable result was obtained after treatment with sulfanilamide administered with rest periods over several months

SULFANILAMIDE THERAPY IN ACTINOMYCOSIS E M MILLER and E H FELL, J A M A **112** 731 (Feb 25) 1939

In an 11 year old boy, who had a swelling in the abdomen, spontaneous rupture of the swelling occurred In the contents liberated onto the skin, granules of Actinomyces were demonstrated In spite of treatment by means of thymol, potassium iodide and roentgen rays, the process extended, the patient rapidly lost weight and recovery was considered improbable Miller and Fell then instituted sulfanilamide therapy, and within a week's time improvement was noticed Treatment by sulfanilamide was continued for almost ten months, at the end of which time the boy had completely recovered

DERMATITIS DUE TO BUTYN H J PARKHURST and J A LUKENS, J A M A **112** 837 (March 4) 1939

A 2 per cent solution of butyn was instilled into the eye of a 49 year old woman for local anesthesia A dermatitis of the lids developed, which in two days caused the eye to be swollen and shut The condition responded to treatment and was entirely gone in a week Patch tests elicited a positive reaction to butyn and negative reactions to other possible allergens

SULFANILAMIDE TREATMENT OF ERYSIPELAS J NELSON, H RINZLER and M P KELSEY, J A M A 112 1044 (March 18) 1939

During the first six months of 1937, at Bellevue Hospital, New York, Nelson, Rinzler and Kelsey treated 344 patients with erysipelas by means of administration of sulfanilamide in addition to routine nursing and medical care. Comparing the results obtained by that treatment with those obtained in a series of 4,473 patients with erysipelas treated during 1930 through 1936 by methods not including sulfanilamide, the authors show that sulfanilamide decreased the average duration of the disease and lowered the mortality. In the series in which sulfanilamide was given, the mortality was 2.62 per cent, in contrast to 8.4 per cent in the control series. The mortality in children was reduced from 19.7 per cent in the control series to 12.9 per cent in the patients to whom sulfanilamide was administered.

SYPHILIS AND THE LAW, WITH A DISCUSSION OF THE FALSE POSITIVE BLOOD SEROLOGIC TEST J H STOKES and N R INGRAHAM JR, J A M A 112. 1133 (March 25) 1939

Some of the pitfalls which may follow legislative attempts to control venereal diseases are discussed by Stokes and Ingraham. They stress the need for careful study before laws are enacted. No single test or single procedure uncontrolled or unchecked should be used as a basis for a diagnosis of syphilis, including even the dark field identification of *Spirochaeta pallida*. Serologic syphilis may have no significance for public health, while a patient with a primary lesion still in the seronegative stage may be a public danger of the first magnitude. There is no absolute definition of noninfectiousness, and at present there is no means of attaining it infallibly. Provisions for the changing status of a patient with the institution of treatment should not be incorporated in laws, the decision as to fitness is rather an individual problem. The possibility of a false positive reaction to the serologic test for syphilis should be remembered. The source of the report, the time of withdrawal of the blood and the presence of intercurrent and especially of febrile infections are all important factors in the investigations of the positive report. The clinical examination in the doubtful case must be carefully performed by one familiar with the stigmas of congenital syphilis and with the physical signs of invasion in the acquired form of the disease.

AN OUTBREAK OF ANTHRAX INFECTION IN MINKS WITH INFECTION OF A RANCH OWNER H PINKERTON, J A M A 112.1148 (March 25) 1939

Pinkerton reports an outbreak of anthrax in a herd of minks which proved rapidly fatal to more than half. Several were infected in a second herd. The infection was traced to a common source of horse meat from which positive cultures were readily obtained. The owner of the first ranch became infected three days after pelting the last of his minks. Treatment consisted of serum in repeated doses and of neoarsphenamine. Recovery was prompt. No previous records of this infection in minks had been made.

SPONTANEOUS FEVER THERAPY IN NEUROSYPHILIS F E WEATHERBY, J A M A 112.1248 (April 1) 1939

A woman of 31 became disorientated, had convulsions and showed symptoms of tetany, without previous symptoms. There was an associated hyperpyrexia, the temperature reaching 106.4 F (rectal). The Wassermann reaction of the blood and that of the spinal fluid were strongly positive. The colloidal gold reaction of the spinal fluid was 5553100000. Therapy with tryparsamide was started on the third day and improvement in the condition of the patient began shortly afterward. After ten days, the patient was symptomatically well and subsequent laboratory

examinations showed that the syphilitic process had subsided. The rapid clinical improvement without residual mental symptoms is attributed by Weatherby to the spontaneous fever as well as to subsequent antisyphilitic medication.

THE CEMENT BURN ITS ETIOLOGY, PATHOLOGY AND TREATMENT J M MEHERIN and T P SCHOMAKER, *J A M A* **112** 1322 (April 8) 1939

The factors producing cement burns are considered by Meherin and Schomaker to be (1) abrasive action of the concrete, (2) friction made by wearing apparel and the rubbing of contiguous anatomic parts, (3) heat of solution while slaking, (4) the hygroscopic action of lime with its consequent cellular destruction and (5) its corrosive action as an alkali. The authors treated in the past year and a half 60 cement burns, causing a loss of six hundred and forty-two working days. In 20 per cent of the cases infection developed. Prophylaxis consists in thorough lavage of the exposed parts with water immediately after exposure to cement or concrete, in frequent changing of clothing and in the smearing of the frequently involved parts with a heavy petrolatum ointment.

COCCIDIOIDAL GRANULOMA SIMULATING BRAIN TUMOR IN A CHILD OF FOUR YEARS B P STORTS, *J A M A* **112** 1334 (April 8) 1939

Storts reports the case of a girl aged 4 years in whom symptoms developed over a period of six months suggesting a tumor of the brain. An exploratory operation revealed a large cyst in the cisterna magna with thickened arachnoid. *Coccidioides immitis* was shown in stained sections. Some improvement followed the operation, and sulfamidamide therapy was given. Death, however, occurred after two months. The autopsy revealed a recurrence of the tumor at the base of the brain and a small nodule in the right lung. This is the first case of coccidioidal granuloma reported from Arizona.

DERMATITIS FROM ORTHODICHLOROBENZENE J G DOWNING, *J A M A* **112** 1457 (April 15) 1939

Downing reports the sensitivity of a glazier to a solution in which window sashes had been dipped. This sensitivity the author proved by observing the reaction when the substance was dropped on the skin. In a similar manner the harmful ingredient was demonstrated to be orthodichlorobenzene, a substance which has become industrially important in the past few years as a solvent and a wood preservative.

COMPLICATIONS DUE TO ARSENICAL THERAPY IN SYPHILITIC PREGNANT WOMEN. REPORT OF SEVEN MATERNAL DEATHS N R INGRAHAM, *J A M A* **112** 1537 (April 22) 1939

By an analysis of the records over a five year period of the antepartum syphilis clinic of the Philadelphia General Hospital, Ingraham found evidence to indicate that with certain patients during pregnancy there is a much greater incidence of reactions to antisyphilitic treatment than with others. This evidence is at variance with the teaching of many who consider pregnancy a barrier to harmful sequelae from antisyphilitic therapy. Attention is drawn to 7 maternal deaths following the administration of antisyphilitic drugs reported from six different sources in Philadelphia since 1931.

CHRONIC ULCER OF THE LEG ASSOCIATED WITH CONGENITAL HEMOLYTIC JAUNDICE E S TAYLOR, *J A M A* **112** 1574 (April 22) 1939

In a woman aged 20 with congenital hemolytic jaundice the presenting symptom was a chronic ulcer of twelve months' duration on the inner side of the left ankle. Sixteen days after splenectomy the ulcer was entirely healed, and nine

months later it had remained so Taylor comments that an ulcer is an infrequent complication but that when present it is extremely obstinate to most forms of treatment except splenectomy, which affords a rapid permanent cure

TEMPORARILY POSITIVE KAHN AND WASSERMANN REACTIONS IN INFECTIOUS MONONUCLEOSIS REPORT OF A CASE J F SADUSK JR, J A M A **112**: 1682 (April 29) 1939

In a student nurse aged 23, there appeared a sore throat, swollen eyes, a nasal discharge and slight general malaise There was a slight elevation of temperature After eleven days a morbilliform eruption appeared and cervical lymph nodes were palpable The leukocyte count was 6,050 with 65 per cent lymphocytes Large cells like those ordinarily present in infectious mononucleosis were observed The sheep cell agglutination test was positive with a dilution of 1 512, later the titer increased to 1 4,096 The Wassermann and Kahn tests showed 4 plus reactions, both became negative in the tenth week of the disease Sadusk, in reviewing the records at the New Haven Hospital, found that during the past seventeen years, of 37 cases of infectious mononucleosis in which the blood was tested by either the Kahn or the Wassermann technic, in 3 the blood gave false positive reactions The incidence of false positivity (8 per cent) was thus less than in two other reported series, which showed false positive Wassermann or Kahn reactions in 16 and 60 per cent respectively

PURPURA HAEMORRHAGICA FOLLOWING USE OF SEDORMID TWO ATTACKS IN ONE PERSON T MCGOVERN and I WRIGHT, J A M A **112** 1687 (April 29) 1939

A white woman aged 57 had taken one-half tablet of sedormid (allylisopropyl-acetylcarbamide) nightly for several months with no ill effects After a lapse of about a month she took a whole tablet Soon afterward she became acutely ill, with chills, fever and excessive thirst, and later a headache developed When after twenty-four hours the patient was observed by McGovern and Wright, many purpuric lesions had appeared on the skin and in the mouth They were of various sizes, flat and raised, and in the mouth some were pedunculated A large hematoma was present on one elbow A capillary fragility test produced 100 petechial hemorrhages in five minutes There was a decided leukopenia, the platelet count, which had dropped to 52,000 per cubic millimeter on the fourth day, rose to 140,000 on the seventh day The vitamin C saturation test gave a normal reading Treatment consisted in the daily intravenous administration of 1,000 mg of crystalline vitamin C (ascorbic acid) in 10 cc of water Recovery was prompt, but a relapse occurred two months later, when she took one-half tablet of sedormid and showed symptoms similar to those noted

SYPHILIS, WITH SPECIAL REFERENCE TO THE INCIDENCE IN RELATIONSHIP TO AGE GROUPS AND STATUS OF THERAPY AT THE DATE OF INFECTION G H. HANSMANN, J A M A **112** 1796 (May 6) 1939

The experience of Hansmann in four sections of the country points to a decided reduction in the incidence of syphilis in the general population He recently studied at the Milwaukee Children's Hospital the serologic reactions of a series of 3,800 children under 13 years of age and parents, and found that the incidence of syphilis in children was 0.27 per cent In the generation of those who acquired their syphilis before the advent of knowledge of the spirochete, the development of important preparations of arsenic and bismuth and the knowledge of the serologic tests, the incidence was approximately 12 per cent Examinations of 4,012 surgical specimens from adults in three years beginning Jan 1, 1936, revealed evidence of syphilis in only 1 instance During the same period 178 postmortem examinations were made, and in 8 instances lesions of syphilis were observed In only 1 instance, however, was syphilis the major cause of death

UNUSUAL LOCATION OF GLOMUS TUMOR - REPORT OF TWO CASES R C GRAUER and J C BURT, *J A M A* **112** 1806 (May 6) 1939

Grauer and Burt report 2 instances in which a glomus tumor developed on the penis. The first patient was a boy of 6 years in whom a grapelike varicosity and a nodule the size of a marble appeared at the site of a bluish discoloration following an injury. The second patient, a man aged 25, had had a small erythematous lesion on the penis since infancy. At 14 years of age he had received a blow on this region, after which the lesion enlarged, assumed the appearance of an angioma, and became painful on pressure. In the first case no pain was experienced.

DERMATITIS FROM INDUSTRIAL CONTACT WITH NICOTINIC ACID R M WATROUS, *J A M A* **112** 2132 (May 27) 1939

Watrous reports the cases of 4 patients who in the course of employment worked with nicotinic acid and shortly afterward had mild degrees of dermatitis on exposed portions of skin. Burning and itching accompanied the rash in 3 instances. Other workers handling nicotinic acid under identical circumstances experienced no trouble.

LEWIS, New York

TWO CASES OF MILIARY LYMPHOCYTOMA OR BENIGN LYMPHADENOID GRANULOMA OF THE SKIN RUPERT HALLAM and H R VICKERS, *Brit J Dermat* **51** 260 (June) 1939. **LYMPHOCYTOMA OF THE FACE** F F HELLIER, *ibid* **51** 265 (June) 1939

Of the 3 cases described, 2 were of the localized type of lymphocytoma and the other of the disseminated type. The condition is uncommon, only 20 to 30 cases having been reported. The essential feature is the occurrence of discrete and nonirritating small translucent subepithelial nodules, which histologically are found to be structures resembling lymph follicles and composed of lymphocytic infiltrates enclosing germ centers. The localized type most often attacks the face, it has occurred in both sexes and at all ages but is more common in women. The lesions may persist for years. In one of the cases, diathermy and refrigeration with solid carbon dioxide gave good results. The blood picture is normal. The lesions must be differentiated from those of such diseases as epithelioma adenoides cysticum and adenoma sebaceum. The name "benign lymphadenoid granuloma of the skin" has been suggested.

DESENSITIZATION IN THE TREATMENT OF MENSTRUAL INTOXICATION AND OTHER ALLERGIC SYMPTOMS J GEBER, *Brit J Dermat* **51** 265 (June) 1939

Among the conditions which Geber lists as manifestations of menstrual intoxication are acne-like eruptions, perifollicular dermatitis, herpes, poppyseed-sized and larger ecchymoses, erythemas, urticaria and bullous dermatitis. These may be accompanied by systemic symptoms. The blood serum is drawn when the symptoms are at their culmination. Its allergenic nature is proved by the method of passive transfer, but the allergenic substance has not been isolated. From 40 to 50 cc of blood is drawn, treated with 0.3 per cent phenol and stored. In the intermenstruum 0.4 cc of the serum is injected intracutaneously every second day at widely separated symmetric areas, and subsequent injections are made in the same areas. There may be mild local or systemic reactions. In general there was mitigation of the symptoms even at the following menses, and a second series usually brought about full desensitization. The antigen is apparently highly specific for the individual patient, for the administration of serum from another person failed to accomplish desensitization. The author does not state the number of patients that were treated.

RATTNER, Chicago

DIPHTHERIA OF THE VULVA IN CHILDREN V A PETROVA, *Vestnik ven i dermat*, 1939, nos 2 and 3, p 71

Attention is called to the fact that in spite of the frequent incidence of diphtheria of the vulva in girls, with its characteristic clinical picture, the diagnosis is frequently missed. The author reports his observations on 13 cases of diphtheria of the vulva in girls 1½ to 8 years of age. The most characteristic symptom seems to him the complete retention of the urine, this symptom was present in 8 cases, while in 5 there was no retention because pain on urination was less severe. Objective signs are edema of the vulva and dryness and a bluish color of the tissues. In some places the tissues are ulcerated and covered with white and gray membranes the removal of which bares a bleeding surface. In cases of more severe involvement there are areas of necrosis. These manifestations are particularly pronounced in the region of the urethral opening, which seems to be the main reason for the painful urination. The discharge from the vulva was bloody in 9 cases. In 3 cases, in which the condition was less severe, the discharge was insignificant and more purulent, and there was no formation of membranes. In these cases the diagnosis of diphtheria was thought of because of the dryness and the cyanosis of the tissue. In another case the discharge was abundant and purulent, but the dryness of the vulva and the fact that one of the other children had diphtheria of the throat suggested a diagnosis of diphtheria in that individual too. In this case there was an associated gonorrheal infection. Another fairly constant sign is enlargement of the inguinal glands. Association with diphtheria of the throat seems to be rare, occurring but once in the author's cases. General intoxication, malaise and even increase in body temperature are frequently absent in diphtheria of the vulva. In the case of 2 sisters, in spite of a laboratory report of "suspicious of diphtheria," a diagnosis of diphtheria was made because of the characteristic picture, the infectiousness of the disease and the improvement following specific treatment. In another case, in which there were only local symptoms and the clinical course was milder, a diphtheroid bacillus was found. The author believes that the diphtheria bacillus may change its morphologic picture and assume the form of a diphtheroid bacillus, which, although considered nonpathogenic, may under favorable conditions produce a pathologic process of the vulva resembling true diphtheria.

In 10 of the 13 cases there was a preceding chronic vulvovaginitis. The author believes that diphtheria of the vulva develops most frequently as a secondary infection superimposed on a still present or on a past chronic gonorrheal vulvovaginitis.

The prognosis is poor only for patients with severe symptoms or for those who are neglected. In only 1 of the author's cases were there severe complications, and in that case there was no associated diphtheria of the throat.

The author reports also 3 cases of diphtheria of the penis, a disease which is much rarer than diphtheria of the vulva. As in the disease in the female sex, there were retention of urine, the characteristic picture of the tissues and a discharge

Society Transactions

MANHATTAN DERMATOLOGIC SOCIETY

MAX SCHEER, M D, *President*

ANTHONY C CIPOLLARO, M D, *Secretary*

May 9, 1939

Minor Congenital Ectodermal Cutaneous Defect in Naevus Linearis Distribution Presented by DR MAURICE COSTELLO

B O C, a girl aged 6 weeks, at birth presented a linear ulceration on the left upper extremity, beginning over the deltoid muscle at the tip of the acromion process of the scapula and running along the external aspect of the left arm, forearm and wrist and the dorsal surface of the second and the third finger. It was widest at its origin, measuring 1.25 cm, and tapered to its narrowest portion at its most distal point, where its width was about 0.25 cm. It healed in two weeks, the resulting linear scar involving the site of the previous defect. The Wassermann reactions of the blood of both the child and her mother were negative. She is the first child, and there was no trauma at her birth, which was normal. There is no family history of congenital anomalies.

DISCUSSION

DR GEORGE C ANDREWS I agree with the diagnosis as presented, because if a child is born with absence of skin over a certain area there is a congenital ectodermal defect. In the dermatologic literature the term congenital ectodermal defect designates a clinical entity and is applied to the condition of patients such as those described by Dr MacKee and me, who have a peculiar facies and absence of cutaneous appendages. In the pediatric literature, however, many circumscribed conditions are classified as congenital ectodermal defects. Dr MacKee and I described only one kind of congenital ectodermal defect, but there are many localized and minor kinds.

DR DAVID BLOOM In this case the name congenital ectodermal defect is appropriate, for, as in most such cases, the condition occurred intrauterum. The other type of condition should be called hereditary ectodermal defect.

DR GEORGE C ANDREWS I think the familial side of ectodermal defects is being stressed too much. If I remember correctly, such conditions occur in families in which there are a great many children, and it is the last one of seven or eight children who has the anomaly. Also, in families that have many children, sometimes the children have many children, and this condition always tends to occur in the last child. It is a sort of degenerative and "worn-out" process. It is not passed on in families as commonly as is psoriasis or epidermolysis bullosa.

DR MAURICE COSTELLO This infant was seen by me the day after her birth. A number of such conditions have been described in the literature and have been divided into two classes, minor and major ectodermal defects. The defect in the case presented would be included in the former group, and congenital ectodermal dysplasia has been described under the heading of major defects. MacKee and Andrews reported cases in which there was absence of the skin of the abdomen.

Others have described similar defects on the knees and elbows. They are seen most frequently on the scalp and on the lateral aspects of the arms and abdomen. Scars present at birth in some of these cases indicate prenatal healing.

Psoriasis and Granuloma Annulare Presented by DR. GEORGE C. ANDREWS

B. W., a white woman aged 19, states that since she was 2 years of age all the nails of her fingers and toes have been thickened and fragile. For many years the process seemed quiescent, then, at the age of 13, it became active again. The patient complained of dandruff for several years. Except for recurrent attacks of rheumatism she has felt well.

When first examined in 1933 all the nails showed thickening, with accumulation of subungual detritus. The distal portions presented a chalklike appearance. There was periungual swelling with well defined erythema and scaling, and long superficial fissures on the flexor and extensor surfaces of the distal phalanges. No vesicles or pustules were noted. The glabrous skin in general was clear.

In June 1937 smooth flat-topped skin-colored papules developed on the elbows. Histologic examination of one of these papules showed decided hyperkeratosis and acanthosis. The corium was the site of a severe acute and chronic inflammatory reaction, with large numbers of polymorphonuclear leukocytes. There were also edema and a few eosinophils. The changes were not those of granuloma annulare or psoriasis. If the clinical picture were that of an annular granuloma, one could only call the condition erythema elevatum diutinum. The pathologic changes were those of localized cellulitis such as is seen about an inflamed follicle, although no folliculitis was noted in the specimen. The only tenable diagnosis was localized granuloma and cellulitis.

In March 1938 a second biopsy specimen was removed, from the region of the left elbow. This section showed hyperkeratosis and acanthosis. The corium showed some thickening of the blood vessels and a moderate increase of mononuclear cells, and there was some edema, particularly in the papillary layer. No histologic diagnosis was made.

In April 1938 a third biopsy specimen was removed, from the right elbow. The section showed hyperkeratosis and parakeratosis. Parts of the granular layer were well developed. In other places the granular layer had practically disappeared. Edema and canthosis were present. The corium contained dilated vessels and was edematous. An intense infiltrate of polymorphonuclear leukocytes was noted, particularly beneath the epidermis, where the leukocytes seemed to form abscesses with deposition of fibrin. The changes were not characteristic of psoriasis, although they were consistent with one form, known as psoriasis osteacea.

Direct examination of the nails and cultural examination showed no fungi. Cultures of material from the tongue and from the stool for *Monilia* gave negative results.

Four successive tests with old tuberculin varying in strength from 1:1,000,000 to 1:25,000 gave negative results. After the last test a fine papular eruption developed on the face, and the patient refused further tests.

Roentgen examination of the long bones of the fingers showed moderately large vascular foramina in the distal third of the left fifth and fourth digits, second phalanx, and the right second and fourth digits, second phalanx. The size of the foramina suggested the possibility of early changes of sarcoid.

Treatment has consisted of unfiltered roentgen rays given weekly in doses of 100 r. The lesions on the glabrous skin have been treated with chrysarobin and other reducing agents, without benefit.

Weekly treatments of the nails by iontophoresis were carried out for seven months in 1934, zinc sulfate being used at the positive pole and sodium salicylate at the negative pole. There was no improvement from this therapy.

Weekly injections of dermatomycol were tried for eighteen months, without benefit.

DISCUSSION

DR DAVID BLOOM I am unable to make a definite diagnosis, but I have the impression that the lesions on the elbows are scars. As they have been present, together with the ungual changes, since infancy, I should consider the whole syndrome a congenital or inherited dystrophy of the skin and nails.

DR FRED WISE Although at present there is no evidence of vesicular or bullous lesions, I believe that the dystrophic form of epidermolysis bullosa as described by Siemens should be kept in mind. It would be of interest to examine the microscopic changes in the elastica.

DR PAUL E. BECHET I do not agree with the diagnosis of granuloma annulare, as in my opinion the appearance of the lesions does not in the least suggest that diagnosis.

DR GEORGE C. ANDREWS I am much interested in Dr. Wise's remarks. However, the lesions on the elbow have changed greatly in appearance. When we made the diagnosis of granuloma annulare we did it from the clinical appearance of the lesions. They were semicircular, definitely raised, slightly pinkish but almost skin colored, with raised coalescent papules around the border much like those of granuloma annulare. Histologically Dr. Machacek thought that was the most likely diagnosis. The changes in this case occur very slowly. Perhaps later we shall be able to establish a diagnosis.

Dermatitis Herpetiformis Treated with Sulfapyridine Presented by DR MAURICE COSTELLO

A C, an unmarried woman aged 21, has had Duhring's disease for four years. She had typhoid fever in 1933. Tonsillectomy was performed in 1936. Pneumonia occurred and was treated with pneumococcus serum five years ago. She has chronic otitis media on the left, accompanied by a discharge. The eruption and the subjective symptoms were typical of Duhring's disease. She also had vesicles on the conjunctival sac, on the nasal and buccal mucous membranes and in the external auditory canal. The itching was intense. The phytopharmacologic index was 62 per cent. She had been treated previously with solution of potassium arsenite U. S. P., 10 drops three times a day, which always controlled the eruption, and sunlight, to which she responded fairly well. Roentgen rays, ultraviolet rays, autohemotherapy, intravenous administration of sodium cacodylate, autogenous vaccine from the stool (from *Streptococcus viridans* and nonhemolytic *Bacillus coli*), sedatives and cowpox vaccination had no therapeutic effect.

A year ago she was given 40 grains (2.59 Gm.) of sulfanilamide daily for ten days without benefit. About April 15, three weeks ago, she was given a 7½ grain (0.48 Gm.) tablet of sulfapyridine three times a day with 30 grains (1.94 Gm.) of sodium bicarbonate. During the first week of this treatment the vesicles began to disappear and the itching was relieved. At the end of the second week the itching, vesicles and bullae had disappeared, even though the dose had been reduced to 2 tablets a day. The dose has been reduced gradually so that at present she is receiving half a tablet every other day.

DISCUSSION

DR ISADORE ROSEN I think the clinical result in this instance is excellent, but I fear that after the drug has been discontinued for two or three weeks the lesions will reappear. That has been my experience.

DR MAURICE COSTELLO Sulfapyridine was tried empirically. The patient had previously been told to avoid sunlight, so that her present prompt remission cannot be ascribed to it.

NOTE—On November 23 there had been no recurrence of the eruption.

Congenital Defects of Skin, Eye and Bones. Presented by DR GEORGE C ANDREWS

J R, a white girl aged 6 years, at birth had all of the lesions which are now present. The child developed poorly, being of small stature and having extremely wide hips. The left eye is much smaller than the right and is affected by congenital glaucoma. The skin has always been excessively dry and mottled by erythematous and telangiectatic patches and by small flat-topped angiomatous papules. On the arms and trunk there are streaked and linear vesicular lesions somewhat suggestive of angioma serpiginosum, especially in the popliteal spaces. On the sides of the trunk, particularly the right, there is notable atrophy in addition to these vascular changes, and the appearance of this area is characteristic of poikiloderma. Along the forearms and upper parts of the arms, particularly on the anterior aspect of the upper part of the right arm, there are cherry-sized and smaller rounded tumor-like masses which are rather soft. These vary from lemon yellow to cream color. Many are distributed in a linear fashion. On the vertex there is an area of total atrophy the size of a half-dollar, and some of the toes are webbed. Roentgen studies have shown that the skull is of normal structure. Measurement between the clinoid processes shows them to be 9 mm apart.

DISCUSSION

DR MAURICE COSTELLO I saw this patient about a week ago. Besides the bizarre lesions mentioned, several fingers are missing, surgical amputation having been necessary because of their flaccidity.

DR ISADORE ROSEN Although I am not able to make a definite diagnosis, I suggest that investigations be directed toward examination of the skull for a disturbance of the pituitary gland. Lesions of this kind are associated with such disturbances.

DR E WILLIAM ABRAMOWITZ The elevated lesions in the axilla have a yellowish tinge, as if there were some lymph fat or elastic tissue tumors of some kind. I think that defect could be classed as a very extensive complex hemangioma.

A Case for Diagnosis (Atypical Erythema Induratum?) Presented by DR PAUL E BECHET

H D, a woman aged 27, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. She states that for two years she has noticed on the posterior aspect of both legs a symmetrically distributed eruption which during that period has been constantly present. The eruption consists of two patches of approximately the same size, 15 cm in diameter. The patches are made up of aggregated red to yellowish papules ranging in size from that of a pinhead to that of a lentil. Some are covered with crusts, others have undergone necrotization and still others are somewhat violaceous. A few punched-out varioliform scars can be discerned. The histopathologic diagnosis was papulonecrotic tuberculid.

DISCUSSION

DR FRFD WISE Though the large lesion looks more like syphilis than tuberculosis, I should accept the diagnosis of a superficial form of Bazin's disease.

DR DAVID BLOOM The edge of the lesions in particular is yellowish red and suggests tuberculosis luposa cutis.

DR PAUL E BECHET There is punctate scarring throughout the lesions. The whole process is superficial, and there are no deep infiltrations. It is Bazin's disease, but the lesions are atypical.

**Erythroderma Psoriaticum Cured with 30 per Cent Sulfur in Petrolatum
Coincident Chronic Lymphatic Leukemia and Recurrent Herpes Zoster
Presented by DR E WILLIAM ABRAMOWITZ**

Mr H R, a private patient aged 55, married, was a cabinetmaker. He was born in Austria but has lived forty years in the United States. His past history is irrelevant except that he had psoriasis about thirty years ago. During this time he has had six or seven outbreaks of a generalized type. The outbreak under discussion was very severe and developed about January. It was accompanied by an infection of the upper respiratory tract.

At this time it was discovered that the patient had an enlarged liver and spleen with enlargement of the inguinal and axillary glands. The blood count indicated chronic lymphatic leukemia.

The exfoliative dermatitis was treated with a sulfur ointment (30 per cent) in petrolatum. The use of the ointment was continued for a little over three months, resulting in complete disappearance of the eruption. At present only a few scattered scaly papules are present on the body. The sulfur seemed to control the itching better than other remedies.

The blood count now shows hemoglobin, 69 per cent (10 Gm), red blood cells 3,700,000 per cubic millimeter, and white blood cells, 38,900 per cubic millimeter, with polymorphonuclears 10 per cent, lymphocytes 86 per cent, monocytes 2 per cent, eosinophils 1 per cent, basophils 1 per cent and normoblasts 1 per cent. The patient is receiving roentgen therapy over the liver and spleen. He is still using the 30 per cent sulfur ointment for the occasional psoriasis papules.

A biopsy specimen taken when the exfoliative dermatitis was present was studied by Dr David Satenstein who thought that it showed typical psoriasis.

Another feature in this case is that the patient has had ten outbreaks of herpes zoster on the right buttock during the past three years. The remains of a recent attack are still present.

DISCUSSION

DR GEORGE M LEWIS: This is a remarkable result. Such conditions have always given me considerable difficulty so far as therapy is concerned. The use of 30 per cent sulfur ointment would seem to be a preferred method of treatment for many types of generalized eczematous eruptions.

DR ANTHONY C CIPOLLARO: May I ask Dr Abramowitz whether he has cleared up ordinary psoriasis with 30 to 40 per cent sulfur ointment?

DR LUDWIG OULMANN: I saw a colleague with psoriasis lasting for thirty years which responded to treatment at intervals. When leukemia developed (from which he finally died) the psoriasis disappeared.

DR ISADORE ROSEN: The frequent association of recurrent herpetic eruptions in Hodgkin's disease is well known. I am not aware of such an association with leukemia.

DR MAURICE COSTELLO: It is not infrequent to see at the Willard Parker Hospital extensive gangrenous herpes zoster varicelliformis occurring in association with Hodgkin's disease. Because of the aberrant vesicles the patients are sent to a hospital for persons with contagious diseases with the diagnosis of varicella.

DR E WILLIAM ABRAMOWITZ: An erythroderma following psoriasis may clear up rapidly or may be persistent, so it is difficult to judge the effectiveness of the sulfur preparation. The eruption in this case subsided under the treatment. The patient found that the concentrated sulfur gave him relief from intolerable itching, whereas other antipruritics failed.

For ordinary psoriasis 30 per cent sulfur ointment is not so effective. This seems to apply also to the so-called pustular types. I tried it in a few cases of parapsoriasis, and it was not successful. I have been using it for pityriasis rosea with good results. Oppenheim tells me that its use has been the standard treat-

ment in Vienna since Neumann's time. Patients with pityriasis rosea use it, and in most cases the eruption clears up in two to three weeks.

In the cases of Hodgkin's disease observed by me, the herpes zoster was accompanied by scattered vesicles. I think that I saw the patient referred to, who had sacroiliac herpes zoster and Hodgkin's disease, proved by biopsy. He also had scattered vesicles on the trunk which the Board of Health diagnostician called chickenpox. I disagreed with that opinion.

The patient presented tonight, according to the hematologists, has definite lymphatic leukemia. The recurrent herpes of the left buttock may be herpes simplex, but on account of the pain that develops with each recurrence may be recurrent herpes zoster.

Epidermolysis Bullosa Hereditaria. Presented by DR. MAX SCHEER

Mr. R., an unmarried clerk aged 35, born in Alsace-Lorraine of Jewish parents, was first seen yesterday at the Mount Sinai Hospital. The condition is said to have been present since infancy. His mother is living and is said to have the same condition, which has diminished in severity as she has grown older. No other members of the family are known to be affected.

The patient's health has otherwise been always good. He had measles as a child. He sweats a great deal, especially his feet and hands. The lesions were at first attributed to trauma in "the cradle." Later, pressure from shoes and tools produced lesions on the feet and hands. These lesions are said to have ranged in size from that of a pea to that of an egg and to have contained clear or bloody fluid. The patient is certain that the frequency of appearance of new lesions is less with the onset of cooler weather.

At present the feet are cool and moist. The soles and sides of the feet and the toes are bluish red. There are areas of callus-like hyperkeratosis on the plantar surfaces of both feet, in the region of the anterior arch, the sides of the feet and the heels are also hyperkeratotic. The toe nails are yellow, opaque and lusterless. There is some maceration between the toes.

There are pea-sized deep-seated hemorrhagic blebs, one on the right foot and one on the dorsum of the foot, just proximal to the web of the great toe. On the mid-dorsum of the same foot is a ruptured bean-sized lesion which contained clear fluid. The left foot shows one lesion on the dorsum, about the size of a pea. The lesions are said to heal in three or four days.

No definite scars are seen on the feet, on the hands or elsewhere. No bullae have appeared on the hands for several months, because the patient has avoided trauma. No lesions have been present at any time on the elbows or knees. No nails have been lost from the fingers or toes.

Since March 1938 the patient has been receiving two intramuscular injections of vitamin C (0.1 mg. each) daily. He is positive that since that time his lesions have been 50 per cent less frequent. Oral administration of the vitamin, according to the patient, was much less effective.

Examination of scrapings for tinea was done but gave negative results.

DISCUSSION

DR. FRED WISE. I do not agree with the diagnosis as presented. I believe that the eruption is due to hyperhidrosis and that the bullous lesions result from occluded sweat gland ducts. By a determination of the hydrogen ion concentration of the fluid from the bullae one might be able to differentiate between sweat and serum.

DR. DAVID BLOOM. As the patient has had this disease since infancy and as the mother has the same disease, the diagnosis of epidermolysis bullosa is to be accepted. Being the simple type which does not leave scars, it is dominant in hereditary transmission. The dystrophic type is transmitted by the recessive mode of inheritance, which explains the fact that in cases of the dystrophic type no other members of the family are usually affected.

Purpura Annularis Telangiectodes Presented by DR ANTHONY C CIPOLLARO

F V, a man aged 35, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He complains of an eruption of eight years' duration, involving mostly the lower extremities. The condition has become progressively worse, and there have been no subjective symptoms. The patient has always been in good general health.

The patient has lesions on the legs and on the medial and lateral surfaces of the thighs. The lesions are purpuric and are arranged either as circles or as parts of circles. Some of the circinate lesions are 1 cm in diameter. The part of the eruption situated on the legs is sharply demarcated. Small areas of atrophy, depigmentation and alopecia are seen. The lesions on the thigh are of the same nature.

DISCUSSION

DR FRED WISE. Although the eruption possesses some of the features of Majocchi's disease, it is difficult to determine the diagnosis after a single brief examination. In cases of Majocchi's disease one usually obtains a history of remissions and exacerbations, sometimes associated with rheumatoid symptoms. It would be desirable to examine the blood vessels for hyaline degeneration.

DR ANTHONY C CIPOLLARO. I saw this patient a few days ago, and the first diagnosis I made was Majocchi's disease. I looked at the man closely and found that he had definite areas of punctate atrophy. The atrophic spots appeared to be the end results of the purpuric lesions. I saw discoid and circinate lesions with central areas of atrophy. The cayenne pepper spots did not impress me, because such spots are found in any purpuric eruption, whether it is purpura simplex, Schamberg's disease or Majocchi's disease. The general health has been good. The patient has no rheumatic manifestations. There have been no exacerbations or remissions. The disease has become progressively worse and more extensive. Tonight the patient shows lesions in all stages of evolution. Clinically I think that this is a case of Majocchi's disease.

Lichen Planus Starting on the Palms Presented by DR LUDWIG OULMANN

A W, aged 54, a machinist working with oil a good deal, noticed an itchy rash on both palms four months ago. The lesions were hard papules, and some showed central depression. The lesions spread over the dorsal sides of the hands to the wrists, then to the sacral region and finally to the arms and trunk. In these regions the lesions are scaly. There are annular lesions and longitudinal lesions showing Koebner's syndrome after scratching. There are white plaques on the mucous membrane as well as papules in his mouth.

The patient was seen by us in February but was sent to a physician who treated him as a "compensation case" for an occupational dermatitis. The patient appeared again yesterday in his exacerbated condition. He blames the oil which he is handling. There is no pigmentation.

DISCUSSION

DR E WILLIAM ABRAMOWITZ. This is one of the most pronounced eruptions of lichen planus with palmar lesions that I have seen in a long time.

DR WILBERT SACHS. There are some lesions on the chest which are smaller, lack the color of the other lesions and might fit in with the picture of lichen nitidus. I suggest a biopsy of material from these lesions as well as from one of the typical lichen planus lesions.

DR LUDWIG OULMANN. I could not see any lesions of lichen nitidus. The patient is convinced that the oil which he handles is the cause of his affliction. It is known that dermatitis lichenoides and Riehl's melanosis occur in persons who work with oils, but this is a case of clearcut lichen planus with oral lesions.

CLEVELAND DERMATOLOGICAL SOCIETY

JOHN A GAMMEL, M D, *President*C G LARocco, M D, *Secretary*JAMES R DRIVER, M D, *Reporter**Feb 23, 1939***Xanthoma Diabeticorum Chiefly Limited to the Palms Presented by
DR W F SCHWARTZ**

M D, a woman aged 51, was first seen in the dermatologic clinic at the City Hospital on Feb 16, 1939, complaining of yellow streaks in the palms. She stated that these had been present for five months. She was known to have had diabetes for nearly three years, which had been controlled chiefly by dietary methods except for a period beginning nine months ago, when insulin was given for three months. She admits that since then she has not followed the recommended diet. About one month after the insulin was discontinued the yellow streaks appeared in the palms.

There is an orange-yellow ribbon-like infiltration in all the flexor folds on the fingers, palms and wrists. A nodule 2 mm in diameter, of similar color, is situated on the tip of the left elbow. There is no surrounding inflammatory reaction. Near the inner canthus on each lower eyelid is a suggestive diffuse yellowish discoloration without induration. Except in these areas the skin and mucous membranes are free from lesions. Examination of the ocular fundi showed no evidence of diabetes.

On Sept 13, 1938, the value for blood sugar was 229 mg and that for blood cholesterol 452 mg per hundred cubic centimeters. Examination of the urine for sugar on Feb 15, 1939, gave a strongly positive reaction.

DISCUSSION

DR E W NETHERTON: I disagree with the diagnosis. I believe this is a case of xanthoma tuberosum multiplex. This type of xanthoma occurring in diabetic patients is not uncommon. It is not true xanthoma diabeticorum. In that disease the lesions are usually small, with small yellowish apices which look like purulent exudate. They usually respond to treatment for diabetes. Xanthoma tuberosum multiplex may occur in a person with diabetes, and the xanthomas may or may not show a response to antidiabetic treatment. The blood cholesterol will be increased in xanthoma diabeticorum provided the diabetes is untreated, while on the other hand it may or may not be increased in xanthoma tuberosum multiplex.

Dermatitis Factitia Presented by DR GERARD ANTHONY DEOREO

R F, a well nourished but neurotic and apprehensive housewife aged 33, presented from the department of dermatology and syphilology, City Hospital, gives a long history of various complaints since 1930. She had a pelvic inflammatory disease in 1932, sacroiliac arthritis in 1933 and an ovarian cyst one year later. Since this time she has appeared periodically in the surgical outpatient department for treatment of "burns" and other minor "accidents."

On the evening of Feb 9, 1939, some sores appeared on her left arm, more appeared on the following morning while she was waiting in the dermatologic dispensary. She was advised that new lesions would appear, which they did on February 14. Two days later several new areas were involved.

The skin is clear except for lesions on the left arm. These consist of bizarre, geometrically shaped excoriations on the forearm, the hand and each phalanx. They are in various stages. There are several fresh erythematous areas, other areas are vesicular, and still others are covered with fresh eschar.

DISCUSSION

DR JOHN A GAMMEL: Has any effort been made to find out why the patient engaged in this practice?

DR GERARD ANTHONY DEOREO: My associates and I have gone into the history carefully, though we did not make her realize that we were suspicious. I think there is ample evidence that her home life is not satisfactory. She has to do a good deal of work, and she has three children. I believe she produces the lesions to obtain sympathy. I haven't ascertained as yet how she produces the lesions.

DR JOHN A GAMMEL: I contend that the process is not hysterical. When one speaks of hysterical cutaneous conditions one refers to eruptions which come on spontaneously. This patient produces the lesions purposely. I prefer the diagnosis of neurotic excoriations, probably produced by her finger nails.

DR H A HAYNES: I do not approve of the diagnosis of neurotic excoriations. When such excoriations occur it is because the patient thinks there is something wrong with the skin. Dermatitis factitia would better describe this disease.

DR GEORGE HASKEL CURTIS (by invitation): I should classify this as dermatitis factitia.

DR JOHN A GAMMEL: No one will object to the statement that the condition is artificial, but it isn't a dermatitis, even in the widest sense of the term.

Pustular Bacterid Presented by DR G W BINKLEY

E I, a man aged 34, in September 1937 had an eruption on the left heel. Several months later a similar process involved the left hand. In July and August 1938 the toe nails of the right foot and left great toe became thickened. Two weeks ago the patient expressed a bead of pus from under several toe nails on the right foot. There has been no itching or pain.

There is a quarter-sized area of scaly skin on the left thenar eminence. The primary element is a deep-seated pustule, which can be seen where the stratum corneum is thin. In other places the corneum is thick. On the left heel and on the lateral edge of the left foot is a similar plaque showing primary subcorneal pustules. Secondary hyperkeratinization is present. The scales are adherent, tough and dry. The inflammatory process spreads peripherally. At times it recedes only to spread again. There is no central clearing of the process. Several nails of the right foot are thickened, and beneath them is dry, yellow detritus.

Cultures on Sabouraud's brain broth and blood agar showed no growth. Direct microscopic examination of scales and of the contents of pustules showed no fungi or bacteria.

Fungicides and superficial irradiation have been used, but no definite improvement has resulted. In fact, the eruption has spread outward on the heel from an area the size of a silver dollar to its present extent (5 by 10 cm).

DISCUSSION

DR C L BASKIN, Akron, Ohio: I should make a diagnosis of pustular psoriasis.

DR JOHN A GAMMEL: There is involvement of the nails. Unfortunately the patient has been so well treated that it is impossible to see what the original con-

dition was However, since the nails look so smooth, I think the process did not go through the entire thickness of the nails, probably only the upper third

DR H J PARKHURST, Toledo, Ohio I believe the possibility of pustular psoriasis certainly should be considered, although the patient is unaware that there has been any eruption in the past It is possible that the changes in the nails may be psoriatic and that the cutaneous lesions may be pustular psoriasis However, I favor more the diagnosis of pustular bacterid with periodic flare-ups and erythematous patches Such conditions are often relieved by tonsillectomy, the tonsils being the common focus of infection However, I feel that in the presence of involvement of the toe nails one should not entirely abandon the possibility of dermatophytosis

DR JOHN A GAMMEL Have any efforts been made to find a focus of infection?

DR G W BINKLEY I have examined the patient's tonsils They showed no particular abnormality, but I shall consult a specialist in diseases of the nose and throat as to whether a tonsillectomy is indicated

Melanosarcoma (Cutaneous Melanoblastoma) Presented by DR HAL ELSON FREEMAN

C H, a man aged 72, is presented from the department of dermatology and syphilology, City Hospital He first noticed growth and enlargement of one of many pigmented nevi on the back five weeks ago A tendency to bleed easily was noted

The lesion, which is in the mid-dorsal region, to the left of the midline, is a bluish black, pigmented, slightly raised area measuring 2 by 4 cm Histologic examination of tissue removed from the center of this pigmented area showed the skin to be resistant to cutting and firm and fibrous to a depth of approximately 1 cm The surrounding skin shows numerous seborrheic keratoses and melanotic nevi

Histologic examination showed the epidermis to be thin and atrophic Near the center of the section was a tumor which invaded the corium It was composed of variously sized and irregularly shaped cells with vesicular or compact nuclei and varying quantities of basophilic granular cytoplasm Some of these contained large amounts of brown granular pigment Other cells had grown out from the main tumor, and small groups of them were observed beneath the basal layer of the epidermis Some had penetrated the epithelium Occasional collections of tumor cells were present in the lymphatics of the corium There was a chronic inflammatory infiltrate along the margins of the tumor

DISCUSSION

DR W. F SCHWARTZ If one has a suspicion that a melanotic lesion is undergoing malignant degeneration, is one justified in taking off the entire lesion when it is as large as this one, or is it permissible to take material for biopsy from the recently growing part?

DR E W NETHERTON I feel that if it is a true malignant growth which has undergone recent degeneration, the probability is that when a clinical diagnosis can be made it is too late to do anything for it Sometimes the clinical impression is wrong, and there is nothing to be lost by doing a wide excision One may possibly save a life that otherwise would be lost If the tumor is a melanoma and is left alone, one knows the ultimate outcome If there are demonstrable metastases, I think it is foolish to do anything in the way of a surgical procedure

Various pathologists differ regarding the taking of biopsy specimens. I believe that if a specimen is taken with a cautery the risk is not great—that is, in a case of ordinary malignant disease. Melanomas are treacherous. I prefer to excise them and then examine them.

DR JOHN A GAMMEL. Some time ago I saw some statistics presented by an English writer on melanomas. He stated that the mortality is 96 per cent. Early radical treatment should improve this rate.

DR C G LAROCO. I believe that any tampering with a lesion of this type should be done with the plan of excising it completely. As such a tumor is highly malignant and tends to metastasize readily and seriously, the safer plan would be to excise it widely and then get biopsy material from the excised lesion.

DR E W NETHERTON. I heard Dr Freeman say that such tumors are supposed to come from the mesoderm. I think it is the accepted opinion at present that melanoblasts arise from cells of nerve sheaths.

DR HAL ELSON FREEMAN. I have read in two recent books that if such a growth is a raised verrucous lesion it usually is a melanocarcinoma. If it is flat or slightly raised, it is probably not epithelial but mesodermal in origin.

DR H J PARKHURST, Toledo, Ohio. In a case of this kind I consider electrocoagulation and intensive treatment with roentgen therapy the method of choice. If metastases have not yet occurred, the growth can be cured. I believe I have cured 2 or 3 patients in this manner.

DR E J ARDAY, Lakewood, Ohio. I do not think there is enough evidence for this diagnosis, and I am inclined not to accept it.

DR H A HAYNS. It is my impression that melanomas are extremely radio-resistant. I had a patient a year and a half ago whom I treated with radiation. A total of 8,000 r was given in a small area, enough to cause complete tissue destruction, at least of the surrounding tissues. The melanoma in the center was more resistant than the normal tissue.

DR H G MISKJIAN. About 1935 I read a paper on melanoma (Seharnagel, I M. *Acta radiol* 14 473, 1933). A physician of Stockholm, Sweden, had collected all the cases of melanoma observed over a number of years. Roentgen therapy had been employed. The diagnosis had been confirmed histologically in each case. The doses had not been high. The results were satisfactory. There was a large percentage of cures. That has puzzled me ever since. It has been absolutely impossible for me to understand how they could get any results with the dosage they used.

NOTE.—I observed, on looking over the article, that a combination of methods was used, including electrosurgery, and not roentgen therapy alone.

Onychia Due to Handling Sugar. Presented by DR C L CUMMER

A R., a woman aged 23, complained of a disease of her finger nails, of two years' duration. It began about two or three months after she started to work in a bakery, where she handled jams and jellies, pressing this material with her bare fingers into baked goods as a filling.

When first seen, on July 18, all the finger nails except those on the thumb and index finger of the left hand were affected. Some were entirely stripped off, others were split and lifted from the nail bed. In some instances the distal portions were detached, in others, the proximal. The paronychium around the involved nails was red, swollen and tender. The detached nail tissue was yellow, and the history indicated that some pus had been present. Except in one or two nails,

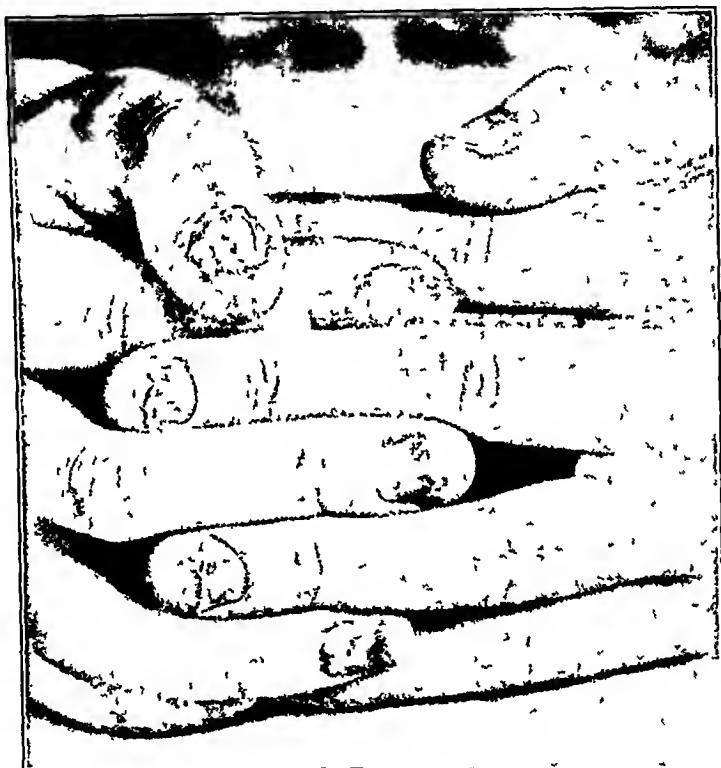
the nail plates were thinner than normal When the nail plate was lifted, heaped-up and granular tissue could be broken away

Microscopic examination of nail tissue showed no mycelium or spores

A photograph is presented to show the condition when first seen The nails at present appear entirely normal

After the patient stopped work the disease responded promptly to treatment with roentgen rays, with compresses soaked in boric acid solution and with boric acid ointment

This condition is described as "sugar onychia" in Prosser White's book (*The Dermatoses or Occupational Affections of the Skin*, ed 3, New York, Paul B Hoeber, 1929, p 318)



Onychia due to contact with sugar

Atrophic Arthritis with Subcutaneous Nodules and Tertiary Syphilis Presented by DR W F SCHWARTZ

J M, a woman aged 57, is presented from the department of dermatology and syphilology, City Hospital She has been troubled with a progressively developing atrophic deforming arthritis, affecting chiefly the small joints of the extremities, for the past five years In the past three weeks two firm, painless nodules have developed in the scalp The patient stated that three years ago she had similar nodules in the scalp, which lasted about three months but disappeared under the influence of massage

In the occipital region are found solitary firm painless nodules measuring approximately 0.75 cm in diameter They are firmly attached to the underlying structures, but the overlying skin does not appear to be affected There are no clinical signs of syphilis

Serologic tests for syphilis gave strongly positive results

Biopsy was not permitted by the patient

Atrophic Arthritis with Subcutaneous Nodules and Pulmonary Tuberculosis Presented by DR W F SCHWARTZ

T C, a man aged 30, is presented from the department of dermatology and syphilology, City Hospital. In the past five years he has had intermittent attacks of arthritis affecting chiefly the joints of the hands, feet, wrists, elbows and knees. The condition was diagnosed as atrophic arthritis. For three years he has had pulmonary tuberculosis. About two months ago three firm, painless nodules measuring from 1 to 1.5 cm in diameter developed in the scalp, and a similar one developed over the right elbow. One of the smaller ones in the scalp was removed for histologic examination. The nodule over the elbow has also been removed for microscopic study.

The nodules are apparently attached to the underlying periosteum. There is no sign of acute inflammation, and the overlying skin shows no change.

Roentgen examination of the skull showed no evidence of exostoses.

Examination of the sputum revealed tubercle bacilli. Serologic tests for syphilis gave negative results.

Histologic examination of the tissue removed showed essentially no change in the epidermis, the chief change being found deep in the corium and in the subcutaneous tissue in both specimens. It consisted of several small focal areas of necrosis, each of which had a striking peripheral zone of radially arranged epithelioid cells. These areas were separated by incomplete bands of newly formed and old fibrous connective tissue cells with surrounding edema.

DISCUSSION OF CASES OF ATROPHIC ARTHRITIS

DR W F SCHWARTZ. A good many diagnoses had been suggested, sarcoid, exostoses and the like, before we had the benefit of the slide.

DR C L CUMMER. Are these nodules regarded as similar to subcutaneous fibroid nodes such as are seen in children with rheumatic heart disease?

DR W F SCHWARTZ. H Keil (*Rheumatic Subcutaneous Nodules and Simulating Lesions, Medicine* 17 261-380 [Sept] 1938) stated the belief that the rheumatic subcutaneous nodules frequently seen in children are essentially the same as the rheumatoid nodules seen in cases like the present one. He dealt with that subject thoroughly. He stated that these nodules may be a sign of an active rheumatic process in children but do not constitute such a sign in the adult condition. Many of the nodules are self limited and may last only a few days to a few weeks at the most and then disappear. These 2 patients point to the fact that subcutaneous rheumatoid nodes are not infrequently seen in the scalp. They usually appear in the articular regions and are believed to be secondary to trauma.

May 25, 1939

Capillaritis Presented by DR BENJAMIN LEVINE

E N, a white woman aged 50, has been under antisyphilitic therapy for the past six years. During the past two years on the lower extremities numerous diffuse purplish noninfiltrated macular patches have developed which do not disappear on pressure. The subjective sensations are slight.

Histologic examination reveals evidence of subacute inflammation, with moderate endothelial proliferation, an increase in the number of blood vessels and a moderate increase of brown granular pigmentation in the basal cell layers.

DISCUSSION

DR H G MISKJIAN I am glad to see that the word capillaritis is becoming more popular I believe the condition in this case is an early form which later will develop into what is usually called varicose dermatitis The newer name for that is purpuric pigmented dermatitis with thickening of the skin Anatomically and clinically the lesions are more of the vascular type than of any other

Mycosis Fungoides Presented by DR IRVING L SCHONBERG

J G S, a man aged 45, has had trouble with his skin for the past thirty-four years The condition originally started as spots over the entire body, which gradually acquired scales He was seen by several dermatologists, who made a diagnosis of exfoliative dermatitis In addition, ring-shaped lesions have developed on the chest He has also noticed tenderness under the left arm and swelling in the lymph nodes of the groins The condition for the past few years has been better in summer

Examination reveals erythematous scaly areas over the face, scalp, back, chest and legs On the chest, in addition to the scaly lesions there are infiltrated violaceous patches, varying in size from that of a quarter to that of a dollar Itching has been slight and occasional From time to time he has noticed small ulcers appearing in the groin

Serologic tests for syphilis gave negative results The hemogram is normal

The patient has been receiving vitamin therapy, has been applying an ointment consisting of 2 per cent salicylic acid in rose water ointment U S P and has been taking starch baths

Histologic examination of two sections showed the epidermis for a distance of about 14 mm to be several times average thickness All but the basal cells were swollen, and the outermost cells in places showed prominent vacuolation In several places there were definite tiny vesicle formations, the largest about 350 by 150 microns There was some round cell infiltration in the thickened epidermis Overlying the epidermis was some desquamated necrotic epithelium The epithelial prolongations of the epidermis were lengthened everywhere, and there were fairly numerous mitotic figures in the epithelial cells, with no extension beyond the basement membrane There were moderate to considerable round cell infiltration and scarring in the upper corium The cutis throughout showed increased reticular connective tissue There were no sebaceous glands, and the sudoriferous glands showed atrophic changes

DISCUSSION

DR J E FISHER I saw the patient about eighteen years ago and made a diagnosis of parapsoriasis The lesions are now more pronounced, but I still offer the same diagnosis

DR I L SCHONBERG I saw this patient about two months ago At that time he presented a scaly condition, more severe than the present one, over the entire body and some infiltrated nodules on the chest The main part of the dermatosis was not infiltrated The diagnosis of dermatitis exfoliativa was made several years ago by Dr J Schamberg, of Philadelphia The condition has progressed somewhat It has never been the source of itching or any discomfort The histologic examination showed some of the early changes that one might find in the premycotic stage of mycosis fungoides He has never had roentgen therapy

DR H N COLE I think I saw the patient a couple of years after I was in practice, before Dr Schamberg saw him I made the same diagnosis, and the patient went to the Mayo Clinic, where the same diagnosis was again made His condition has certainly changed since that time The generalized condition in some

ways makes one think of a nevoid condition or parapsoriasis. The areas on the inside of the right thigh, where he has some lymphangiectasis, resemble those on a patient presented at the Academy meeting in St. Louis last fall. He does have some plaques on the back, about the size of the palm and with a tendency to be elevated at the periphery and to be somewhat depressed in the center, that suggest the beginning of the tumorous stage of mycosis fungoides. When I looked at the slide and saw the sharply defined sleeve-like type of infiltrate, I was inclined to think that the condition might be an unusual type of mycosis fungoides that has developed in a parapsoriasis that has lasted all these years. It is hard to understand why he has had so little pruritus.

DR HUGO HECHT (by invitation). My first impression was that the disease is mycosis fungoides. I saw the patient today for the first time.

Urticaria Pigmentosa Presented by DR BENJAMIN LEVINE

R T, a Jewish woman aged 35, for the past ten years has had distributed over the trunk and extremities numerous brownish and erythematous macules, varying in size from that of a pinhead to that of a pea. On manipulation these areas become darker and papular. At times the condition is intensely pruritic.

Treatment has been symptomatic.

Histologic examination revealed an infiltration of mast cells in the corium, especially near the basal cell layer. The cells were large and spindle shaped, oval, round or polygonal and were separated from the epithelium by normal connective tissue. There was increased pigmentation in the basal cell layer and also in the papillary body.

Urticaria Pigmentosa Presented by DR BENJAMIN LEVINE

M R., a pregnant woman aged 29, stated that eight years ago she noticed a rash, which at times was itchy. The eruption gradually became darker and on friction would become edematous and more extensive.

The lesions are sparsely generalized, discrete and about 5 mm in diameter. Since the patient has become pregnant the eruption has been less pronounced.

Urticaria Pigmentosa Presented by DR BENJAMIN LEVINE

H K, a woman aged 25, for the past four years has had an itching eruption.

Over the chest and back are numerous split pea-sized brown macules, which become edematous after irritation.

Lymphangiectasia of the Vulva with Edema of the Legs Presented by DR FRANK McDONALD

M B, an obese Italian woman aged 52, presented from the department of dermatology and syphilology of the Lakeside Hospital, has symptomless lesions on the vulva of two years' duration. The legs have been swollen for almost twenty years. The swelling in the left leg has been attributed to a fracture, and the swelling in the right leg apparently arose as phlegmasia alba dolens concomitantly with pregnancy.

On the upper portion of the right side of the vulva are ten or twelve grayish vesicopapules, each somewhat smaller than a split pea, grouped together in an area measuring about 2 by 3 cm. There is no evidence of inflammation in the surrounding area. When the individual lesions are opened, a slight serous exudate is obtained. The lower extremities exhibit a pitting edema. There are no scars, varicosities or ulcers, and there is no tenderness.

A blood smear failed to reveal *Filaria bancrofti*.

Histologic examination of tissue removed from a vulvar lesion showed a thick layer of hyperplastic stratified squamous epithelium. Throughout the cutis and in

the rete pegs was a dense infiltration with small round cells, including plasma cells and lymphocytes. There was a moderate amount of fibrosis. There was no evidence of tumor. The lymph vesicles and spaces were greatly dilated.

Hemiatrophy of the Face Presented by DR BENJAMIN LEVINE

E. B., a woman now aged 59, at the age of 18 was struck on the head with a flatiron, and her skull was presumably fractured. The skin was not broken. Four years later she had her first attack of epilepsy. These attacks lasted for a short time and occurred without aura. They were later controlled by anti-syphilitic therapy.

When she was first seen, in September 1932, there was a hemiatrophy of the left side of the face. The skin is atrophic and closely adherent to the bone, with atrophy of the subcutaneous tissue and muscle. There is no paralysis.

The Kline test for syphilis gave a strongly positive result. The spinal fluid was normal.

DISCUSSION

DR H. N. COLE: I have seen several patients with hemiatrophy of the face. However, the condition is not necessarily localized to the face but may involve other parts of the body. In the large proportion of cases there is a history of trauma. Bartlett has written a great deal on this subject. If it occurs early enough, it may even involve bone, and the bone will not grow as much as the corresponding bone on the other side.

DR H. A. HAYNES JR: It is interesting that epilepsy developed in this patient also. A decompression would possibly have prevented the epilepsy.

A Case for Diagnosis (Macular Atrophy? Nonsyphilitic White Spot Disease? Anetoderma Erythematodes of Jadassohn?). Presented by DR BENJAMIN LEVINE

L. W., a woman aged 45, has had numerous white spots on the neck, chest, shoulders and back for sixteen years. The condition progressed until the birth of her last child, ten years ago. The lesions are not itchy or painful.

The individual lesions vary in size from 1 to 5 mm in diameter. They are dead white and atrophic, with great enlargement of the pores, giving a pig-skin-like appearance. The smaller lesions are on the neck, the larger, on the chest and back. There is increased pigment on the right side of the neck.

The basal metabolic rate was —6 per cent. The hemoglobin content was 52 per cent, but the hemogram was otherwise normal. Serologic tests for syphilis gave negative results.

The patient would not allow a histologic examination.

Contact Dermatitis Due to Physostigmine Salicylate Presented by DR H. H. JOHNSON

L. S., a woman aged 59, presented from the department of dermatology and syphilology of the Lakeside Hospital, in February 1937 had a diagnosis of chronic glaucoma made at Lakeside Hospital. She was treated with 1 per cent pilocarpine hydrochloride. Physostigmine ointment, containing 0.5 per cent physostigmine salicylate, was applied only occasionally until Aug. 3, 1937, when she was again given this medication. After one week the eyes and lids became red, and by December 13 there were generalized erythema and scaling of the face. These have persisted, with exacerbations and remissions. On April 15, 1939, an exacerbation of the condition occurred. The ointment was discontinued on April 21, and the dermatitis has been slowly subsiding since that time.

Examination shows a diffuse erythema of the face and neck, with scaling and cracking of the skin. There is moderate edema of the face, especially about the eyes.

The conjunctivas are moderately injected. The optic fundi show glaucomatous disks, and there is an iridectomy window in each iris.

Patch tests with 0.5 per cent physostigmine salicylate gave strongly positive reactions, with 1 per cent pilocarpine hydrochloride, negative, with 0.5 per cent pontocaine hydrochloride, slightly positive, and with 1 per cent phenacaine hydrochloride, negative.

DISCUSSION

DR H. H. JOHNSON: Contact dermatitis from physostigmine salicylate ointment has been reported infrequently in the literature. Atropine is commonly described as producing an irritation of the eyes. In several recent textbooks on dermatology no mention of physostigmine as a possible irritant is mentioned.

Congenital Syphilis Presented by DR BENJAMIN LEVINE and DR I. L. SCHONBERG

W. J. B., a Negro boy aged 12 years, whose parents are known to have syphilis, presents Hutchinsonian teeth, a saddle back nose, a high palatine arch and thickened periosteum over the tibiae. The eyes appear normal. His mentality is good, but he is undersized for his age.

Serologic tests for syphilis were strongly positive.

DISCUSSION

DR J. R. DRIVER: I asked the child whether he had ever had sore eyes. He said that his eyes had been inflamed and red on two or three occasions several years ago. On close examination there is no evidence of interstitial keratitis. However, I believe it would be interesting to have the cornea examined by the slit lamp. In many instances in which nothing is seen grossly, the telltale scarring is evident on slit lamp examination.

Scleroderma Presented by DR BENJAMIN LEVINE

B. M., a man aged 47, noticed hardening and thickening of the skin of the left forearm the latter part of July 1937.

It became progressively more extensive until it involved all of the left shoulder and extended in a broad band, 8 to 10 cm. in width, over the lateral portion of the brachium and the dorsal surface of the forearm, terminating on the dorsum of the index finger.

The skin is smooth and shiny with increased pigmentation and mottled pigmentation over the areas in which the scleroderma first appeared. The lesions also are firm and slightly edematous, with firm attachment to the underlying tissue, resulting in a hidebound condition.

He had received twenty-six injections of solution of posterior pituitary U. S. P., of 1 cc. each. Six months after these injections the condition showed signs of regressing, with decrease in stiffness and edema.

Histologic examination of tissue showed that the papillary bodies were flattened and obliterated. The horny layer was increased. There was degeneration of the connective tissue bundles. The blood vessels showed endoperiarteritis and phlebosclerosis. The hair follicles and glands in certain areas have disappeared.

Papilloma of the Palate (Probably Due to Red Mercuric Sulfide [Cinnabar]) Presented by DR BENJAMIN LEVINE

S. H., a man aged 52, has had diabetes for the past eighteen months. For the past year he has been conscious of "lumps" on the hard palate. He has been wearing a red dental plate.

There are numerous enlarged follicular openings on the hard palate. On some areas there are pinhead-sized to split pea-sized erythematous soft papillomatous growths.

Histologic examination showed acanthosis, spongiosis and marked elongation of the papillary bodies. There was thickening of the malpighian layer, with hypertrophy of the interpapillary pegs.

DISCUSSION

DR J R DRIVER I have observed several patients with stomatitis due to plates, and in the cases I have had, patch tests with the plate itself on the skin have given positive results. I should suggest that patch tests be done in this case.

Radiodermatitis of the Hands with Malignant Degeneration. Presented by DR H N COLE and DR J R DRIVER

A A B, a dentist aged 60, has had an irritation of the fingers of both hands for five years, which he attributed to contact with procaine hydrochloride. He has noticed for several years warty growths on his fingers. One month ago he scraped one of these lesions off accidentally, and the area thus traumatized has ulcerated and has not healed. For a period of more than fifteen years he has taken roentgenograms of teeth.

The thumbs, index fingers and middle fingers of both hands are primarily involved. They show numerous keratoses, with dryness and some atrophy of the skin. The nails on these fingers are brittle and show longitudinal striations. On the dorsum of the middle finger of the right hand is an ulcer 4 by 3 cm., with indurated granulomatous edges.

Histologic examination of a specimen taken from the edge of the ulcer showed that the epidermis was thickened, and in one situation there was ulceration, the ulcer being occupied by tumor. Beneath the epithelial layer was a tumor which had invaded the skin and subcutaneous tissues. It was not encapsulated, and there was obvious local invasion. The tumor was composed of atypical epithelial cells, and in some places there were degenerate epithelial pearls. No intercellular bridges were seen. There were also foci of degeneration and necrosis of tumor cells, which gave some areas a network appearance. The individual cells tended to be round and moderately large with abundant cytoplasm, pleomorphic and hyperchromatic nuclei showing numerous atypical mitotic figures. Surrounding the tumor were moderate fibrosis and infiltration with small round cells. There was no necrosis or hyaline thrombosis of the blood vessels, and no eosinophilic infiltration was seen. A diagnosis of well differentiated squamous cell carcinoma was made.

DISCUSSION

DR HUGO HECHT (by invitation) In Prague about fifteen years ago (in 1924) I observed a similar condition in a young man. He was treated with roentgen rays. Two years later the ulcer was cancerous. The finger was removed, and then the right arm. The development was from 1922 to 1929. He had about seven operations. Radium may be tried, but surgical treatment is better.

DR H N COLE Dr Driver and I have seen several dentists who told in their history of holding dental films in the mouths of patients while taking roentgenograms of teeth. The practice is not carried on so much at present, but it is surprising how often it was done in the past. For many years the patient presented today held films in mouths with his thumb. Apparently this finger got caught in the process and even got a larger dose than the thumb. Typical radiodermatitis, changes in the nails and an ulcer on the back of the hand have developed.

Since the tendon is involved in this case, it will be impossible to cure the process by any method except amputation. I know of no carcinoma on the hands in which the tendons were involved that was cured by irradiation. The finger will be amputated tomorrow.

The question has been raised as to how this condition can be radiodermatitis without telangiectasia. I saw a dentist this morning who has had a similar condition, without telangiectasia, which is now cleared up.

Pityriasis Lichenoides Chronica Presented by DR GEORGE H. CURTIS and DR E. W. NETHERTON

S. S., a Jewess aged 32, noticed an eruption first on her face about six years ago and shortly afterward on the extremities, it rather rapidly spread to involve the trunk. There have been no subjective sensations, except for dryness of the skin. The eruption appears to be more pronounced in the spring and fall. All sorts of treatment have been tried without benefit.

The eruption is most intense on the extremities, the face and the lower part of the trunk. On the face there is a slightly scaly reticulated erythema showing telangiectasia on diascopic pressure. Scattered over the trunk and extremities are many split pea-sized flat scaling macules with a yellowish tint, while other lesions are papular, especially on the extremities. The scales on the papules are difficult to remove and leave a pink moist surface underneath. The axillary folds and the upper extremities show a bluish red reticulated erythema and telangiectasis. In the network are pinpoint-sized to pinhead-sized deep red papules simulating those of lichen planus. Distally the network thins out and consists of sparsely distributed erythematous scaly macules, somewhat lichenified. The lower extremities show similar changes. The mucous membranes are normal.

General physical examination showed only normal conditions. The hemogram and the urine were normal. Serologic tests for syphilis gave negative results.

Histologic examination of sections taken from lesions on the hip and the upper part of the arm showed in the horny layer a definite parakeratosis but no corresponding granular layer. The prickle cell layer was acanthotic, with spongiosis and several vesicles in early stages. Small round cells had invaded the epidermis, except where the edema of the papillae had invaded the germinal layers, the basement membrane was intact.

A number of the papillae were considerably flattened below the acanthosis, but many showed edema and round cell infiltration, especially around dilated capillaries.

The upper part of the corium showed edema and small round cell infiltration continuous with that of the papillae. About dilated blood vessels the edema and cellular infiltration were most marked. The infiltrate consisted almost entirely of small round cells. No eosinophils, neutrophils or plasma cells were seen.

The deep corium and the subcutaneous tissue were unaffected.

A section including pinhead-sized papules from the brachium showed similar but less extensive changes, except that the blood vessels of the corium were more numerous and dilated, and there was hyperkeratosis, without parakeratosis.

DISCUSSION

DR J. E. FISHER: I had the privilege of seeing this patient five years ago, and the picture has not changed much since that time. I agree with the diagnosis as presented. She had not responded to any treatment at that time, including various topical applications. I made a metabolism test, the result of which was normal.

DR H. N. COLE: I think that in some places on this patient's body the discrete papules are rather characteristic of pityriasis lichenoides chronica. Considering the amount of telangiectasia and atrophy, one should keep in mind the possibility of Jacoby's disease as time goes on.

DR HUGO HECHT (by invitation): I have seen the best results with six months of sunshine and sea baths. I think Florida has the right climate. In Prague there are two or three families who have this condition. Every summer they go to the seashore, but in the winter the eruption recurs.

DR J R DRIVER What I have to say is speculative I think it might be interesting to investigate whether the condition is a deficiency disease I had in mind the possibility of perhaps using riboflavin in the treatment

DR GEORGE H CURTIS We presented this case for two reasons The first reason is that the patient insists that the eruption improves in the summer, seems to be worse in the spring and is bad in the fall and throughout the winter With that history in mind I should like to ask whether it might be advisable for her to invest in an ultraviolet lamp The second reason is that Juliusberg in his article says that often the condition when on the extremities must be differentiated from poikiloderma The eruption on the arms shows some telangiectasia, the overlying epidermis is atrophic and it is deep red The epidermis and probably the upper part of the cutis seem to be atrophic On the sides of the neck the eruption has a retiform character and looks like parapsoriasis variegata, particularly as illustrated in Ormsby's textbook (Ormsby, Oliver S Diseases of the Skin, ed 5, Philadelphia, Lea & Febiger, 1937, p 284)

Necrobiosis Lipoidica Diabeticorum Presented by DR E W NETHERTON and DR GEORGE H CURTIS

G C, a housewife aged 37, was presented before the society on Jan 19, 1939 (ARCH DERMAT & SYPH 40 455 [Sept] 1939)

She is shown at this time because (1) the lesions have enlarged and are clinically more suggestive of Boeck's sarcoid and (2) although her diabetes has been rigidly controlled for more than six years, new lesions have appeared and the old ones have enlarged

On May 24, 1939, the blood cholesterol was 146 mg per hundred cubic centimeters and the blood sugar (fasting) was 128 mg per hundred cubic centimeters

New histologic sections have been stained for fat and elastic fibers and showed the typical histologic changes of necrobiosis lipoidica diabeticorum

Syphilitic Macular Atrophy Presented by DR BENJAMIN LEVINE

A H J, a Negress aged 27, states that a rash developed over the entire body four years ago She consulted a physician, who made a blood test, which gave a strongly positive result She received injections in the arm and in the hip for one year

On the trunk and extremities there are numerous split pea-sized to coin-sized atrophic areas

Serologic tests for syphilis gave strongly positive results

Histologic examination of tissue showed that the surface epithelium was somewhat thinner than average In the corium there was some increase in the relatively acellular fibrous tissue The cutaneous glands were diminished in size and number In the upper layers of the corium there was some perivascular infiltration The section was stained for elastic fibers by Weigert's method and showed no appreciable diminution in their number

DISCUSSION

DR H N COLE Syphilitic macular atrophy is not common, but it does occur, particularly in Negroes Histologic examination does not show evidence of syphilis The condition is probably the result of some trophic factor

DR I L SCHONBERG I should like to ask Dr Cole in how many patients that present this trophic macular atrophy he would expect to find neural changes in the cord

DR H N COLE I am not in a position to answer that, but I think it would be an interesting question to investigate

DR GEORGE BINKLEY In the cases of syphilitic macular atrophy I have observed, the examinations of the spinal fluid have given normal results

DR BENJAMIN LEVINE The patient just presented has normal spinal fluid

*June 15, 1939***Necrobiosis Lipoidica Diabeticorum** Presented by DR GERALD ANTHONY DEOREO

L R, a woman aged 29, is presented from the department of dermatology and syphilology, City Hospital. She has had diabetes mellitus since 1933. The disease has been controlled by diet and insulin. About two years ago a lesion developed on the anterior surface of the left leg, which she states resulted from a bruise. It has gradually increased in size.

At present it is about 3 cm in diameter. The border is violaceous and the center yellowish, with numerous telangiectases.

The value for blood sugar recently has varied from 87 to 187 mg per hundred cubic centimeters. A urinalysis showed a faint trace of sugar.

Histologic examination showed that the epidermis was thin, the papillae decreased in number and the follicles larger than usual. In the deep layers of the corium the blood vessels and glands were surrounded by fuzzy collars of lymphocytes, a few large mononuclear cells and occasional polymorphonuclear leukocytes. Deep in the corium there were a few strands of young connective tissue sprinkled with chronic inflammatory cells and the collagen fibers were swollen and fragmented. In such areas a few pyknotic inflammatory cells were seen. The results of histologic examination were consistent with the clinical diagnosis.

Livedo Racemosa in a Syphilitic Patient Presented by DR GERALD ANTHONY DEOREO

M S, a woman aged 26, was seen at the City Hospital in 1932, at which time a diagnosis of petit mal was made. Serologic tests for syphilis gave strongly positive reactions, and she received twelve injections of arsphenamine and twelve of a bismuth compound. She failed to return for further therapy until April 20, 1939, when she came in complaining of blue mottling of her skin.

On the flexor surface of the forearms and to a lesser degree on the trunk and the lower extremities there is a coarse network of purplish blue mottling. The eruption seems to follow the course of underlying blood vessels.

Neurologic examination gave negative results. Serologic tests of the blood and spinal fluid for syphilis now give negative reactions.

DISCUSSION

DR H N COLE: This patient, although she shows no evidence of syphilis, has the disease. Ehrmann has called attention to certain conditions with syphilis as a background. About twenty years ago I saw a German boy with early syphilis. He was given treatment for about two years. At that time continuous therapy was not in use, and he went back to Germany. He stayed there for about four years. On his return to the United States he came in to see me because of a peculiar eruption on his body. He had one of the most extensive eruptions of livedo racemosa I have ever seen. I looked him over carefully for evidence of syphilis. The spinal fluid was normal, but I interpreted the process as a relapse. I gave treatment for a short time, and he disappeared from observation. I have not seen him since.

DR GERALD ANTHONY DEOREO: On looking back I found that 35 cases of one type or another of livedo racemosa have been reported in the *ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY*. In only 3 of these, however, was the condition attributed to syphilis. In 2 cases there was a positive Wassermann reaction, but the condition was not ascribed to syphilis. In the other cases tuberculosis and rheumatism played a part. There was disseminated lupus erythematosus in 2 cases.

Trophic Ulcers of the Face and Neck Due to Syringobulbia Presented by
DR W F SCHWARTZ

R E, a woman aged 40, is presented from the department of dermatology and syphilology, City Hospital. She has complained of numbness of the left side of the face for a little more than five years. Shortly after the onset she burned herself with a heat lamp in the region of the ear. Since then there have been recurrent superficial ulcers above and behind the left ear. These healed spontaneously, leaving an atrophic scar, only to be followed by ulceration. About six months ago the numbness in the face progressed down to the left side of the neck, the left shoulder and eventually the right shoulder and the radial aspects of both arms and hands. The recurrent superficial ulcerative lesions have extended to involve the left side of the face and neck.



Trophic ulcers of the face and neck due to syringobulbia

The area of anesthesia corresponds to the distribution of the sensory part of the fifth cranial nerve, especially the maxillary and mandibular branches, and also to that of the cervical nerves down to the fourth. There is dissociation of sensation, touch being better preserved than pain and temperature. The sensory defect is now spread bilaterally over both shoulders and down the radial surfaces of both arms and is associated with early interosseous atrophy. The tongue shows some atrophy. The pharyngeal reflexes are sluggish. There is rotary nystagmus to the left. There is no muscle "tendon" reflex change.

On the skin there are confluent atrophic and hyperemic scars above and behind the left ear as well as on the lower part of the left cheek and the side of the neck. These are the results of the recently healed ulcers. The left external ear shows atrophy. The crusted ulcers before healing occurred are shown in the accompanying illustration.

The hemogram revealed moderate secondary anemia. Serologic tests for syphilis gave negative reactions. The spinal fluid was normal.

Healing was rapid after the use of an ointment containing Aloe vera.

DISCUSSION

DR W F SCHWARTZ. One of the first reasons for presenting this patient is that it is unusual to see trophic ulcers in this region. The most important reason for showing her is that there was considerable difficulty in recognizing the condition as trophic ulcer in its early stages. There would be bizarrely shaped superficial ulcers above and behind the ear on one visit, and on another these would be healed and there would be some in a different region. Dermatitis factitia was the diagnosis made at that time. It was not until the disease had extended to the front of the ear, the patient complained bitterly of numbness of the face and atrophy of the ear was noticed that a lesion of the central nervous system was suspected.

DR JOHN E RAUSCHKOLB. It is interesting that neurologists see such conditions frequently and recognize them readily. I have labored with this patient for two years before I arrived at a diagnosis, and then I did so only with the aid of neurologic consultation.

Facial Paralysis Due to Early Syphilis of the Central Nervous System, Granuloma Inguinale. Presented by DR W F SCHWARTZ

J M, a Negro aged 25, is presented from the department of dermatology and syphilology, Cleveland City Hospital. Nine months ago he had a penile sore which was diagnosed as primary syphilis. He received no treatment at that time. Three months later he suddenly had crossed hemiparesis, of the left side of the face and of the right arm and leg. The paralysis of the extremities lasted about one week, but the facial paralysis did not improve. Two months ago the patient was admitted to the City Hospital because of another penile sore, which had been present a little more than one month. This has been diagnosed as granuloma inguinale. In the past two months three injections of a soluble bismuth preparation and thirteen of mapharsen have been given. The facial paralysis has improved considerably.

At present the patient presents a granulomatous ulcer on the shaft of the penis, from which Donovan bodies have been demonstrated. At the time of his admission to the hospital there was decided paresis of the facial muscles on the left as well as of the muscles of the forehead on the same side. There was no evidence of involvement of any of the cranial nerves other than the seventh. The muscle tone, the deep and superficial reflexes and the sensory changes of the extremities were essentially normal and equal. The skin was free of eruption.

Serologic tests for syphilis gave strongly positive reactions. The Wassermann reaction of the spinal fluid was 1 plus in 0.5 cc and 4 plus in 1 cc. The cell count was 5 per cubic millimeter, and the mastic curve, 2210000000. The Pandy reaction was 1 plus.

DISCUSSION

DR H N COLE. There are many cases of Bell's palsy not related to syphilis, but one should keep in mind the possibility of Bell's palsy of syphilitic origin. Some years ago there were 2 patients in the hospital at the same time with a syphilitic type of Bell's palsy. Since then I have not seen any until I saw this Negro with early syphilitic paraplegia and Bell's palsy. The disease does not always respond readily. It is much like other types of Bell's palsy in that respect.

Juvenile Tabes Dorsalis. Presented by DR W F SCHWARTZ

B V, a girl aged 16, is presented from the department of dermatology and syphilology, City Hospital. In December 1934 she first sought treatment at the Lakeside Hospital for occasional headaches and failing vision. Serologic tests of

the blood gave strongly positive reactions, and the Wassermann reaction of the spinal fluid was also positive, and with the mastic curve was 21110000000. The patient had had no previous therapy for syphilis. Her father and two siblings, aged 13 and 22, have been examined and showed no physical or laboratory signs of syphilis. Two other siblings, aged 25 and 28, have not been examined. The mother, who is 51, has syphilis but shows no physical or laboratory signs of involvement of the central nervous system. There have been no miscarriages.

During the past four years the patient has received the following medicaments: acetarsone for seven months (Jan 11 to Aug 16, 1935), neoarsphenamine, twenty-eight injections, bismuth subsalicylate, eighty-two injections, and pyrifer (a non-specific protein mixture of extracts of fever-producing bacteria from certain non-pathogenic stocks), three courses, with a total of thirty-six treatments.

The patient is well developed and well nourished, with no structural stigmas of congenital syphilis. An intelligence test indicated normal average intelligence. The pupils were dilated, irregular and fixed to light. The deep and superficial reflexes of the upper extremities were normal. All deep reflexes of the lower extremities were absent, but there was no change in the superficial reflexes. The sense of position was slightly impaired, and there was slight ataxia, but a Romberg sign could not be demonstrated. Consultation with physicians of the genitourinary department resulted in a tentative diagnosis of tabetic bladder. There has been no incontinence.

Serologic tests of the blood and spinal fluid for syphilis gave negative results at this time.

DISCUSSION

DR H N COLE. I think there is a tendency to take the position that one cannot expect much improvement from treatment of juvenile tabes and dementia paralytica. Some patients, however, improve remarkably under antisiphilitic therapy, particularly fever therapy. I do not think it makes a great deal of difference whether one uses artificial fever therapy, malaria or a bacterial foreign protein preparation.

DR C L CUMMER. I wish to support Dr Cole's statement. I remember a boy who had well marked juvenile tabes before the introduction of fever therapy. He is now married, the father of two children and perfectly normal. He looked hopeless about ten years ago.

DR W F SCHWARTZ. Such cases are distinctly uncommon. So far as I know, this patient is the only one with juvenile tabes registered in the dermatologic clinic at the City Hospital. The symptoms of juvenile tabes dorsalis are not as severe as those of the acquired form. Even in cases in which there are full-blown physical signs that the disease has affected the vital organs, such as cord bladder, there are very few symptoms.

DR E W NETHERTON. It is interesting to note that this child shows syphilis and is between two other children who show no signs. We do not know about the two oldest children, but this would be a rather high incidence of nonsyphilitic babies from an untreated syphilitic mother. I wonder whether the mother was treated during any of her pregnancies.

DR W F SCHWARTZ. When the patient reported at the Lakeside Hospital in 1935, syphilis in the family was discovered for the first time. The mother has latent syphilis without involvement of the central nervous system.

Mycosis Fungoides Presented by DR W F SCHWARTZ

E. D., a man aged 65, was first seen at the City Hospital one year ago, at which time he complained of a painless mass protruding from the skin of the right groin, which he stated had been developing for three or four months. He also had a generalized exfoliating dermatitis which had developed gradually over twenty years and which he stated had been called "psoriasis." There had never been any pruritus. A few small soft flat nodules were seen on the abdomen and

in the axillary region. The mass in the groin, as well as these nodules, resolved rapidly under the influence of roentgen therapy. During the past year similar soft nodules, either discrete or arranged in circular groups, have appeared on the trunk, and these have likewise responded rapidly to four or five roentgen ray treatments (80 r each). Pruritus has now become a prominent symptom. The exfoliation has become possibly a little more extensive.

Except for the palms and soles, almost all surfaces of the body are affected by a brownish red, slightly scaling dermatitis. It is universal except for several areas where it is interrupted by configurate patches of normal skin. There are a few soft flat nodules scattered throughout the eruption.

The liver, spleen and lymph nodes are not enlarged. Roentgen examination of the chest showed no evidence of parenchymatous infiltration in the lung fields or enlargement of the mediastinal lymph nodes. The hemogram was normal, and serologic tests for syphilis gave negative reactions.

Six specimens were removed for histologic examination, one from the sternal bone marrow and five from the skin. The sternal bone marrow was normal. Tissue taken from one of the soft nodules as well as that taken from a non-infiltrated scaling patch showed no evidence of lymphoblastoma and was reported by the pathologists as showing only chronic inflammation. Sections of tissue taken from the mass in the groin were reported as lymphoblastoma of the skin. The tissue from the tumor in the groin showed the epithelium to be the seat of mild parakeratosis and varying degrees of acanthosis. The epithelial pegs were elongated, slender and irregular. The cells composing some of their tips were separated by edema and cells of the type to be described as occurring in the corium, so that the basal layer of a considerable portion was fuzzy and extremely irregular. There was diffuse cellular infiltration in the corium, extremely well delimited to the papillary and superficial portions of the subpapillary layer. The cells comprising the exudate consisted chiefly of lymphocytes, with smaller numbers of large mononuclear cells, eosinophils and a few cells which could not be identified. One or two mitoses were seen, but no giant cells were present.

Tissue removed recently from one of the cutaneous nodules showed that the squamous epithelium was absent in most places. The remaining fragments showed severe inflammatory hyperplasia. The surface of the tissue was necrotic, and an acute purulent exudate was present in this region. In the underlying tissue severe inflammatory changes were also present, but these were more subacute, as was evidenced by numerous eosinophils. Granulation tissue was present in places. In addition, there were numerous large, irregular cells arranged in a diffuse manner. These cells had large, vesicular and in general round nuclei with one or more prominent nucleoli. A few of these cells were multinucleated. Mitotic figures were fairly frequent. Many of the cells contained clear vacuoles in their cytoplasm. There were no definite structural formations. A stain for mucin gave negative results. A stain for reticulum gave positive results.

DISCUSSION

DR H. A. BRUNSTING: I should like to ask about the therapy.

DR H. N. COLE: Lomholt has reported some rather favorable results from the use of chaulmoogra oil for mycosis fungoides. At the Montreal meeting of the American Dermatological Association, Dr Hiram C. Miller mentioned a case of mycosis fungoides in which he gave fever therapy and obtained a severe response. It almost killed the patient, but the mycosis fungoides disappeared. That, of course, is an isolated instance.

DR W. F. SCHWARTZ: I have considered fever therapy but was not particularly impressed by the isolated report in the literature of a single case in which use of the Kettering hypertherm produced temporary benefit.

DR E. W. NETHERTON: I should like to ask Dr Work whether from the standpoint of the pathologist he would say this is Hodgkin's disease.

DR JOHN WORK (by invitation) The pathologic concept of mycosis fungoides differs from the clinical concept. My experience has been that conditions which are typical clinically of mycosis fungoides may be any of a number of lymphoblastomas. Some are Hodgkin's disease, some, sarcoma. I think the condition in the present case must be regarded as a form of Hodgkin's disease or reticulum cell sarcoma. One sees Hodgkin's disease affecting the liver, spleen or lymph nodes. I am not going so far as to call this definitely Hodgkin's disease, but reticulum cells and many other abnormal cells are present. There are a few giant cells similar to Reed-Sternberg cells. The mere fact that one calls the condition Hodgkin's disease does not mean that it is not mycosis fungoides. In the light of my experience and the pathologic experience of others, I think mycosis fungoides is a characteristic type of cutaneous disease that may be due to any one or a number of lymphoblastomas. In some cases it may be caused by reticulum cell sarcoma and in some by Hodgkin's disease.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

EUGENE F. TRAUB, M.D., *Chairman*

LOUIS TULIPAN, M.D., *Secretary*

April 28, 1939

Symposium on Syphilis

Recent Periostitis Developing During Treatment of Late Syphilis. Iridocyclitis (Old) with Secondary Glaucoma. Presented by DR. LEO SPIEGEL.

E. S., a woman aged 38, presented from Bellevue Hospital, has an infection of unknown duration. It was first discovered on Jan. 24, 1938, when the patient came to Bellevue Hospital with an active iridocyclitis of the left eye believed to be of syphilitic origin when examined in the ophthalmic department. On January 25 the Wassermann reaction was 4 plus. The patient had no treatment prior to this time. Since that day she has received thirty injections of a bismuth preparation and twenty-five injections of arsenicals (sixteen of arsphenamine and nineteen of mapharsen) in the syphilis clinic. The iridocyclitis responded promptly to anti-syphilitic treatment.

On Feb. 10, 1939, while under treatment, the patient began to complain of an aching pain in both shins, worse at night and in the early morning. Exercise did not make it worse. Repeated examinations in the clinic revealed no tenderness. Roentgenograms of the legs showed moderate periosteal thickening of the lateral aspects of both tibias, suggestive of syphilitic periostitis. The patient was receiving mapharsen at the time of the onset of her pains. Owing to severe gastrointestinal reactions, the doses of arsphenamine were reduced from 0.3 Gm. to 0.2 Gm., early in the course of treatment. The highest dose of mapharsen tolerated was 0.03 Gm.

The Wassermann reaction of the blood has been 4 plus at all times since Jan. 25, 1938. The results of tests of the spinal fluid on February 15 were normal. Roentgenograms of the heart and the aorta were normal. Roentgenograms of the long bones are presented for inspection.

The case is presented in order to find the cause of the periostitis.

DISCUSSION

DR. EVAN W. THOMAS (by invitation) I have never encountered a case like this. I believe the condition is late syphilis. In every case of late syphilis of the bones that I have observed, however, there has been an osteitis along with the periostitis.

DR E W ABRAMOWITZ Syphilis of the eye and bone is not uncommon in Negroes. No doubt this patient has some periosteal involvement. When treating a patient with medicaments containing bismuth, unusual complications sometimes develop. Bismuth rheumatism and deposits of bismuth in the bones may occur. In cases in which the bone symptoms do not seem to respond to the bismuth preparation used, a complete change in treatment should be made. Bismuth should be discarded and mercury given by injection. If the patient is intolerant to arsenamine, it might be omitted, or perhaps a different type of arsenical might be used, a pentavalent rather than a trivalent arsenic compound. The point I am interested in is whether Dr Spiegel can rule out a possible deleterious effect on the bones from the bismuth itself.

DR ISADORE ROSEN I wonder whether this patient received any iodides during the rest periods. It might be advisable to stop the intravenous and intramuscular medication for the present and administer iodides in medium-sized doses. The administration should be followed with a roentgenogram, to show the effect.

DR LEO SPIEGEL I have observed patients with syphilis who had severe pains in the joints and muscles after long courses of treatment with a bismuth preparation. I agree with Dr Rosen about administering iodides, but before that I should give the patient three or four injections of sodium thiosulfate and nothing else, to see if the pains disappear. The pains may be due to the continued use of bismuth although the roentgenograms show evidence of periostitis due to syphilis.

DR EVAN W THOMAS (by invitation) Since the roentgenograms have been examined, which was only about two weeks ago, all treatment has been stopped. The patient had had alternate courses of treatment with a bismuth preparation and with mapharsen, beginning with the bismuth compound. I ordered mercuric succinimide in daily injections, but she refused to come in more than once a week. I doubt if she is intelligent enough to take mercury injections properly. I think that stopping arsenical treatment for the present and giving only iodides will be helpful, or perhaps mercury injections could be tried in spite of her lack of good cooperation.

Osteoperiostitis of the Femur Presented by DR LEO SPIEGEL

F F, a woman aged 40, with a syphilitic infection of about seven years' duration, is presented from Bellevue Hospital. A routine Wassermann test on Dec 20, 1938, gave a 4 plus reaction. For four years before this the patient had been complaining of pain in the right thigh, which was worse at night. She had had no treatment before December 20, when she was admitted to the syphilis clinic.

Examination of the spinal fluid on Jan 11, 1939, gave negative results. Roentgenograms of the heart and the aorta on January 18 were normal. Roentgenograms of the long bones on January 11 showed osteoperiostitis of the medial aspect of the proximal half of the right femur.

Meningomyelitis Syphilitica with Muscular Atrophy Presented by DR LOUIS CHARGIN

J M, an Austrian aged 26, is presented from the Central Social Hygiene Clinic of the Department of Health, with Dr Luis Perelman. The patient says that he has not had syphilis. In February 1938 he noticed progressive weakness and clumsiness of the hands, wasting of the muscles of all four extremities and numbness of the hands and feet. A diagnosis of progressive muscular atrophy was made by a neurologist. For a time the patient was treated with electrotherapy but without benefit. He was admitted to Mount Sinai Hospital on July 22, where examination revealed bilateral wrist drop, foot drop, definite atrophy of the muscles of the extremities, profound weakness of the distal muscles of the extremities and complete absence of deep reflexes except for the pectoral muscles. Vibratory sensation was absent from the iliac crests down, and there was diminished sensation of pain, touch and temperature over the fourth lumbar

and the first sacral segment bilaterally. Lumbar puncture showed a partial block. Examination of the spinal fluid showed 135 mononuclear cells and a total protein of 88. The Wassermann reaction of the spinal fluid was 4 plus, and the colloidal gold curve was 1122211000. The Wassermann reaction of the blood was also 4 plus. The patient was discharged from Mount Sinai Hospital on September 2, unimproved.

The patient was next admitted to the Meinhardt Clinic on October 20, where examination showed the motor system to be as previously described, the Romberg reaction positive, the deep reflexes absent and the sensory system as previously described, with, in addition, hypalgesia to pinprick on the ulnar aspects of both upper extremities. The Biernacki and Abadie signs were positive. Examination showed no evidence of abnormality of the cranial nerves except that the pupils were unequal, the right being larger than the left. The libido is decreased, and the patient has erotic dreams and disturbances of the bladder.

There is definite proof of involvement of the posterior column and degeneration of the anterior horn cells. A diagnosis of syphilitic meningomyelitis appears to be justified. To date the patient has received ten injections of silver arsphenamine and fourteen injections of a bismuth preparation, with no apparent improvement.

DISCUSSION

DR LEO SPIEGEL. I should like Dr. Perelman to tell whether the patient has improved.

DR LUIS PERELMAN (by invitation). The therapy has not been effective. The man consulted a physician because he had had an accident, after which a weakness of the arms developed. The presenting symptom was weakness of the arms, with wasting away of the muscles. He was taken to a specialist, and a diagnosis was made of progressive muscular atrophy. I presume that at that time he had no sensory changes, but they are evident now. His symptoms then were due to lesions resulting from degeneration of the anterior horn cells. This is not a case of tabes. The subjective symptoms oscillate, but objectively the patient does not appear improved. I believe that the pathologic process is vascular and that the lesions will eventually lead to occlusion of the vessels. In that case the changes will be irreversible and the result of treatment questionable. All that can be hoped for is an arrest in the progress of the disease. He has enough cells still intact so that he can use his extremities to the extent he does. With physical therapy these muscles may be saved, and if the antisymphilitic treatment is continued, the process may not progress. The textbooks describe good responses to treatment in such cases. The therapy was started a little late, and that may be the reason why it has been ineffectual. I have never encountered a case like this and therefore cannot give an opinion as to what the results might have been had the therapy been started earlier.

At a conference of neurologists where this patient was presented, there were some suggestions as to therapy. Attention was drawn to the fact that many muscles are still intact. There was not much hope expressed for the possibility of reversal of the syndrome. The active pathologic change is not likely to be reversed. The patient will be referred to the Neurological Institute of New York where the physicians may have some further ideas as to therapy. The suggestion of fever therapy will have to be deferred, because the patient's defenses are at a low ebb and the reaction would be too severe.

DR LEO SPIEGEL. When was the spinal fluid examined?

DR LUIS PERELMAN (by invitation). In August 1938.

DR LEO SPIEGEL. That was a long time ago. While this man has been treated with silver arsphenamine, he also should have been given sodium iodide intravenously in large doses. An active pathologic process is shown by the increased number of cells in the spinal fluid. The spinal fluid should be examined every three months, and if there is no favorable response in six months following

the combined courses of arsenicals, bismuth preparations and sodium iodide, and if the patient is otherwise in good physical condition, fever therapy should be tried

DR LUIS PERELMAN (by invitation) I should like to be optimistic, but I have seen the patient once a week, and I believe his condition is getting worse I believe the therapy has been adequate He has been given the routine therapy that the physicians of the department of health prescribe in cases of neurosyphilis Outside of a hospital I believe nothing more could have been done without exposing him to danger He has had rather severe reactions at times to silver arsphenamine The examination of the spinal fluid was made six months ago, but it was not repeated because the man is weak and is an invalid most of the time Plans are being made to have him hospitalized as soon as possible

Tertiary Syphilis Transverse Myelitis Following Administration of a Bismuth Compound Presented by DR A BENSON CANNON

A DeG, an Italian aged 41, is presented from Vanderbilt Clinic He states that he had gonorrhea and a questionable chancre in 1919 Four intravenous injections were given at that time No intramuscular injections were given He had no further treatment until he was admitted to Vanderbilt Clinic in April 1931 On admission the Wassermann reaction of the blood was 4 plus He complained of severe continuous and throbbing headaches, located mainly in the right parietal region Examination showed that the pupils reacted to light and in accommodation but the ankle and knee jerks were overactive, otherwise the results of the examination were negative Treatment was begun with the administration of bismuth preparations, and two injections were given, on April 30 and on May 7, 1931 Following the second injection a transverse myelitis with complete paralysis of the lower extremities developed The patient was admitted to the New York City Hospital and there regained partial use of his legs He is now able to walk with the help of a cane but has not been able to return to his former occupation of taxi driver The Wassermann reaction of the spinal fluid has remained 4 plus since the first examination in 1931 The Wassermann reaction of the blood is now 2 plus with an alcoholic antigen and 3 plus with a cholesterolized antigen Treatment has consisted of one hundred and twenty injections of a bismuth preparation fifty injections of old arsphenamine, twenty injections of tryparsamide and sixteen Swift-Ellis injections

Examination at the present time shows equal and active pupils, slight leukoplakia of the mucous membrane opposite the last upper molar on the right side hyperactive knee jerks and ankle jerks and a normal heart The lungs and abdomen are normal

The case is of particular interest because of the transverse myelitis which followed only two injections of a bismuth preparation

DISCUSSION

DR HERMAN GOODMAN Were there any clinical or serologic observations prior to the injection of the bismuth preparation which would lead one to suspect the possibility of injury of the nervous system?

DR EVAN W THOMAS (by invitation) What is the nature of the transverse myelitis? Is it due to an inflammatory lesion of the cord or to a vascular condition?

DR FRANK E CROSS (by invitation) I do not believe the bismuth compound had anything to do with the transverse myelitis I think the development of the condition just after the injections was a coincidence

DR L C RUBIN (by invitation) Were there any sensory changes? Did the patient have any trouble with the sphincters of the bladder or rectum? What is the diagnosis of transverse myelitis based on?

DR HENRY D NILES I also question the diagnosis There is no statement in the history about a colloidal gold test or about testing for ankle clonus or for the Babinski or Romberg sign I think these are all necessary

DR. LUIS PERELMAN (by invitation) I should not venture a diagnosis on the basis of the summary on the history card. I should like to know if the patient has any pathologic reflexes or an upper motor neuron or a lower motor neuron syndrome.

DR. JAMES L. MILLER On admission the patient had a positive Wassermann reaction of the blood and of the spinal fluid. The transverse myelitis was probably due to the bismuth administered, but it was a syphilitic myelitis, precipitated by the bismuth in the same manner as a Herxheimer reaction.

Tertiary Syphilis Aneurysm of the Ascending Portion of the Aorta. Presented by DR. JAMES L. MILLER

Mrs. L. J., a Negress aged 33, was admitted to Presbyterian Hospital on June 4, 1935, complaining of pain and "thumping" in the right side of the chest for two months. These symptoms began after a severe cold. The patient also complained of cough, anorexia and the loss of 10 pounds (4.5 Kg). She had nocturnal dyspnea but no edema of the ankles. Physical examination showed a slight tracheal tug, a difference in blood pressure between the two arms (150 systolic and 90 diastolic on the right side and 120 systolic and 90 diastolic on the left side) and an expansile pulsating mass at the right second interspace. A harsh systolic murmur was heard at the apex and the aortic area. Roentgenograms and fluoroscopic examination showed a saccular aneurysm of the ascending portion of the aorta. The Wassermann reaction of the blood was 4 plus.

The patient was given fifteen injections of a bismuth preparation intramuscularly and iodides orally. The aneurysm was wired by Dr. Blakemore in the Presbyterian Hospital on two occasions in 1935. A small portion of the aneurysm still remained active, and this was rewired in 1936. The patient has received about seventy injections of a bismuth preparation intramuscularly, accompanied by the iodides, in the four years since the aneurysm was first wired. No arsphenamine has been given. The patient has remained free, as determined by physical and roentgenographic examination. The aneurysm has remained stationary in size, and no new aneurysms have developed. The Wassermann reaction of the blood is now negative.

DISCUSSION

DR. JAMES L. MILLER The patient has had no pain or edema of the ankles or severe dyspnea. She is able to return to work and does not feel that she has any particular trouble. The case demonstrates how easily the diagnosis might have been made earlier. The condition of her husband, who had had a positive Wassermann reaction, had been diagnosed as syphilis seven years before the patient came to the hospital. She had had three miscarriages, at seven, at five and at three months, and the diagnosis of syphilis might have been suspected then.

Tertiary Syphilis Aneurysm of the Ascending Portion of the Aorta Presented by DR. LESLIE P. BARKER.

Mrs. E. R., a Negress aged 46, is presented from Vanderbilt Clinic. She has had increasing dyspnea for the past twenty-six years, but her condition has remained about the same for the past six years, during which time she has been unable to climb stairs or do any manual labor. She was told in 1923 at St. Luke's Hospital that she had syphilis and received about twenty intravenous injections and forty intramuscular injections at that time. She was admitted to Vanderbilt Clinic in 1931, complaining of dyspnea, cough and substernal pain. Examination revealed an aneurysm of the ascending portion of the aorta, about 8 cm. in diameter. She was given antisyphilitic treatment with bismuth preparations and iodides, and after twenty injections of a bismuth compound small doses of arsphenamine were given. Repeated roentgenograms showed enlargement of the aneurysm, and there was a continued increase in symptoms. The aneurysm was wired by Dr. Blakemore in 1935, and within ten months all the substernal pain had disappeared, the cough had improved and the patient was able to walk eight

blocks without exhaustion, whereas previously she had been able to walk only two blocks. She has continued to improve since that time.

The Wassermann reaction of the blood and the observations on the spinal fluid have been normal since she was admitted to Vanderbilt Clinic.

DISCUSSION

DR EVAN W THOMAS (by invitation) In what percentage of cases of this kind does surgical intervention fail to relieve pain or other symptoms?

DR LESLIE P BARKER Success of the operation depends on the type of aneurysm treated. The saccular type with a very small mouth is the ideal type for wiring, because the flow of blood in the sac is very slow, and it is easier in this type to obtain a clot large enough to obliterate the aneurysmal sac than in the fusiform type, in which the flow of blood is so rapid that it is difficult to obtain clotting.

DR HERMAN GOODMAN What is the fatality of this operation?

DR JAMES L MILLER There have been about 19 patients, 5 or 6 of whom died subsequent to the operation. However, the condition was far advanced in them, and the operation was performed in the days when the technic was first introduced. There is a certain amount of reaction as a result of the heating of the wire. That reaction is considered good, however. There is a certain amount of damage to the surrounding wall, but that can now be controlled, and a certain amount is considered a good thing, because fibrosis occurs afterward. At first, however, the operation apparently resulted in several untoward results, with death occurring in the first five days after operation. The technic has been improved now. Dr Blakemore has recently reported his results (Blakemore, A H, and King, B G. Electrothermic Coagulation of Aortic Aneurysms, *J A M A* 111 1821 [Nov 12] 1938).

Aortitis, Aortic Regurgitation, Aneurysm of the Thoracic Aorta Presented by DR LOUIS CHARGIN

B J, a Negro aged 59, is presented from the Central Social Hygiene Clinic of the Department of Health, with Dr L C Robin. The patient had a penile sore thirty-four years ago which was treated by chemical cauterization. He says that he did not have an eruption. A routine serologic test a year later gave a negative result. About five years ago the patient began to complain of pain in the lower part of the left side of the chest, in the axillary line, accompanied by dyspnea. These attacks increased in frequency. Three years ago the Wassermann reaction of the blood was 4 plus. He received antisyphilitic treatment, consisting of eight injections in the arm and twenty-six in the hip during 1936 and 1937. The pain, however, has not been relieved and is practically always present. There are moderate dyspnea and palpitation on exertion. Since 1937 the patient has been receiving injections of a bismuth preparation and of potassium iodide.

Physical examination shows a well developed but thin elderly man. The heart is enlarged at the apex, downward to the sixth left interspace and outward to the anterior axillary line. There are no thrills or shocks. A soft diastolic murmur is heard best over the aortic area to the right of the sternum at the second interspace. A double murmur is heard at the apex. The pulse rate is regular. The blood pressure is 150 systolic and 90 diastolic in the right arm and 140 systolic and 90 diastolic in the left arm. The pupils are equal, and there is no tracheal tug. Examination of the lungs shows a palm-sized area of dullness with suppressed breath sounds posterior to the left of the spine at the level of the angle of the scapula. The liver is palpable 2 fingerbreadths below the costal margin. There is bilateral pretibial edema, more evident on the right side.

Fluoroscopic and roentgenographic examinations showed the heart to be enlarged in the transverse and oblique diameters. In the left anterior oblique

view the cardiac shadow extended beyond that of the spine, indicating left ventricular enlargement. The myocardial tone was impaired. The aorta was diffusely dilated, as manifested by obliteration of the right aortic distance and by broadening of the supracardiac shadow to the left. In addition, there was a moderate fusiform dilatation of the descending aorta, and in the left anterior oblique portion there was noted, arising from the posterior wall of the midthoracic aorta, a saccular aneurysm the size of a tangerine. Pulsation in the latter was not increased.

DISCUSSION

DR L. C. RUBIN (by invitation) The patient is doing well under treatment with bismuth preparations and potassium iodide in courses, with rest periods in between. He is still working, but at a job at which he sits down. He was formerly a laborer.

DR E. W. ABRAMOWITZ Every once in a while a roentgen examination shows sacculation of the arch or of another portion of the aorta, while the patient has practically no symptoms of aortic involvement. There was a patient recently at the Gouverneur Hospital with a great enlargement of the descending portion of the arch of the aorta. He had no pain and had been taking treatment at the syphilis clinic with no ill effects. He was admitted to the hospital for some other condition. Such patients apparently can carry on light work even though their illness is considered serious.

DR I. ROSEN These 3 cases of aortic aneurysm should impress on the physician who treats syphilis the importance of early roentgen examination of all patients with the disease. In the treatment of aortic aneurysm it is important to outline a form of therapy which is mild and is carried on interruptedly over a long period. I have made it a plan not to give these patients any arsenicals intravenously, and I am satisfied with giving a bismuth preparation or mercury intramuscularly and iodides during the rest periods.

DR L. C. RUBIN (by invitation) We make routine fluoroscopic examinations of all the syphilitic patients at the clinic. I think one point that should be mentioned in the routine treatment of these patients is the necessary reduction of their activity, which is as important as the administration of drugs.

Erb's Spastic Paraplegia, Primary of the Optic Nerve Presented by DR LEO SPIEGEL

G. S., a man aged 50, is presented from Bellevue Hospital with a syphilitic infection of unknown duration. The patient first noted slight difficulty in walking in 1931, at which time a positive Wassermann reaction of the blood was observed at Bellevue Hospital. However, the patient did not report for antisyphilitic treatment. In November 1938 he began to notice stiffness in the muscles of the right leg, described as a drawing feeling in the muscles. This gradually became worse and spread to the left leg. He came to Bellevue Hospital on December 31 because of a spastic gait. He also stated that he had first noticed poor vision in the left eye about Dec 1, 1938.

Physical examination showed that the pupils were equal and fairly regular and reacted to light and in accommodation. Both optic disks were slightly grayish, and the outer temporal margin of the left disk showed slight pallor. Sensation (touch, temperature and vibration) was normal. The biceps and triceps jerks were slightly hyperactive. The ankle and knee jerks were strongly hyperactive, the right being greater than the left. There were bilateral ankle clonus and patellar clonus on the right. There was a positive Babinski sign on both sides. Abdominal and cremasteric reflexes were present. The abductor muscles of both legs were very weak, the right being weaker than the left. The gait was spastic, more on the right side than on the left. On Feb 24, 1939, the ocular examination showed no central scotoma. The color sense was good with artificial light. The

perimetric fields showed interesting quadrant defects involving the upper nasal portion of the right retina and the lower and upper temporal portions of the left retina

On Dec 27, 1938, the Wassermann reaction of the blood was 4 plus On Jan 30, 1939, examination of the spinal fluid showed the Wassermann reaction to be 4 plus with 1 cc and 0.5 cc and plus-minus with 0.1 cc The cell count was 0, there was no globulin and the colloidal gold curve was 0000000000 Roentgenograms of the heart and aorta were normal

DISCUSSION

DR EVAN W THOMAS (by invitation) I never expected to encounter such an unusual case Spastic paraplegia is listed in the diagnostic index but is rarely seen I think this patient presents about as near the textbook picture of this condition as one can get, both in onset and in physical signs Whether the condition is due to syphilis or not I leave to the members It is certainly included among the syphilitic manifestations in the spinal cord A few cases in which autopsy has been performed are described in the literature The same type of pathologic changes are described in the lateral pyramidal tracts that are seen in the dorsal columns in *tabes dorsalis* The changes have been ascribed to syphilis because there has been associated syphilis in some of these cases, but syphilis has not been present in all instances There have been 1 or 2 cases in which autopsy was performed in which a positive Wassermann reaction was not obtained and in which the results of the examination of the spinal fluid were negative This man's condition came on gradually When seen in the clinic he had a spastic gait which could be differentiated from an ataxic gait The abductor muscles in spastic paraplegia are always weaker than the adductors He has a bilateral Babinski sign and bilateral ankle clonus, with patellar clonus on the right He has, in addition, primary atrophy of the optic nerve, which has never been described in association with spastic paraplegia, so far as I have been able to find out in my perusal of the literature When the patient was first examined, on Jan 23, 1939, both disks were grayish, not the typical white disks of primary atrophy of the optic nerve I was slightly skeptical as to whether he had true primary atrophy He has been seen by several physicians, all of whom have come to the conclusion that the condition is a definite primary atrophy with unusual visual fields The vision is worse in the left eye than in the right He has been under treatment only since February 1, and I cannot say that there has been any improvement one way or the other He says he is better He received a bismuth preparation and then pentavalent arsenic I have come to the conclusion that in many of these patients there is a tonic effect from the pentavalent arsenicals The patient says he feels better, yet there is no improvement in the condition of the spinal fluid or it may even be worse I should like to hear a discussion on the value of pentavalent arsenicals in syphilis and especially in *tabes dorsalis*, because I wonder if *tabes dorsalis* is not a meningovascular syphilis due to involvement of the meninges and vessels at the roots and if it is not a very different thing from the parenchymatous form seen in *dementia paralytica* I offer that as a possibility From a study of our charts I can say that the pentavalent arsenicals are of dubious value in the vascular and meningovascular types of syphilis, but I believe they are of value in the parenchymatous type of syphilis of the central nervous system known as *dementia paralytica*

DR LEO SPIEGEL When *tabes dorsalis* is observed early in a patient and the various tests on the spinal fluid show active inflammatory reactions, it is my custom to use at first the trivalent arsenicals The inflammatory reactions in the spinal fluid in these cases show an increased cell count, a definite increase in globulin and protein and various degrees of positivity with a quantitative Wassermann test Unfortunately, tests for protein and globulin are not done routinely in examining the spinal fluid The so-called tests for globulin, such as the Pandy, the Nonne-Apelt and the Noguchi, are indefinite and inaccurate and give no information as to the extent of the pathologic process The proteins should be

tested for by accurate methods, such as the Exton-Rose test, and the turbidities read with suitable instruments. Of the trivalent arsenicals, I, as well as many other observers, prefer silver arsphenamine. This preparation has a somewhat crystalloid structure and supposedly penetrates the meningovascular barrier more readily than the other trivalent arsenicals. It has therefore been my custom to start treatment in these cases, as well as in cases of meningovascular syphilis, with silver arsphenamine and then with old arsphenamine, giving two courses, one of each. Courses of intramuscular injection of bismuth preparations and intravenous injections of sodium iodide are given between the injections of arsphenamine. According to some observers (Moore and others), sodium iodide also penetrates the meninges more readily than potassium iodide when given by mouth. After the aforementioned therapy, I invariably use the pentavalent arsenicals. This remedy has been used for the past four years with gratifying results in many instances. In the cases of so-called "burnt out" *tabes dorsalis*, when the tests of the spinal fluid are negative, no form of antisyphilitic therapy is of benefit. Supportive tonic treatment is then of some help, as the patients are often below par and undernourished.

DR LUIS PERELMAN (by invitation) I should like to ask Dr. Thomas what the status of the upper extremities is and if any other cranial nerves are involved. Are there any sensory changes? What are the serologic changes of the spinal fluid?

DR EVAN W. THOMAS (by invitation) Sensations of all types are normal. The biceps and triceps reflexes are hyperactive, but there is no clonus. The pupils are regular and react well to light. There is no involvement of the cranial nerves except that of the optic nerve. One of the ophthalmologists suggested that the peculiar quadrant defects might represent a lesion in the optic tract which might be due to a gumma, but the others seemed to think the condition was truly a primary atrophy of the optic nerve. There are no signs referable to the dorsal columns. The patient has been examined very carefully neurologically. The only neurologic signs present are pyramidal tract signs. The abdominal and cremasteric reflexes are present. The Wassermann reaction of the spinal fluid was 4 plus with 1 cc. and 0.5 cc. and plus-minus with 0.1 cc., and the colloidal gold curve was flat. The same type of curve is often found in patients with *tabes dorsalis* with involvement of the posterior column when the activity has begun to die and the reflexes are already absent.

DR LUIS PERELMAN (by invitation) Clinically the condition could be multiple sclerosis. Serologic changes are found in the spinal fluid of patients with multiple sclerosis. The description of Erb's spastic paraplegia as found in the textbooks, as Dr. Thomas pointed out, is probably rare clinically. It is likely that the condition would have been considered multiple sclerosis if there had not been the serologic changes and I had not been conscious of neurosyphilis. Was the possibility of multiple sclerosis discussed at all?

DR EVAN W. THOMAS (by invitation) Three neurologists saw the patient, and the question of multiple sclerosis was always brought up, but not a single one would entertain that diagnosis because they were able to demonstrate only the pyramidal tract signs and the atrophy of the optic nerve. Every one agreed that the condition was a spastic paraplegia due to a disease of the upper motor neurons. The question arose as to whether this was due to syphilis. In view of the fact that the ophthalmologists concluded the condition was a primary atrophy of the optic nerve due to syphilis and that there was a definite positive Wassermann reaction, the disease was considered to be syphilis. There may be other changes in the spinal fluid in multiple sclerosis, but there is not a positive Wassermann reaction.

DR ISADORE ROSEN The case is interesting because of the pupillary observations. According to the history, the pupils were normal, and it is unusual to find primary atrophy of the optic nerve, in my experience, without pupillary disturbances.

DR EVAN W THOMAS (by invitation) The man is not totally blind I believe that the visual acuity was 20/200 on the left and 20/100 on the right In my experience it takes almost complete blindness to cause absence of the pupillary reflexes

DR LUIS PERELMAN (by invitation) I want to contribute some information which would bear out what Dr Thomas has said In a number of patients examined by the board of health who had various degrees of primary atrophy of the optic nerve, functionally intact pupils have been found Even in patients with only light and shadow vision left, there was a normally reacting pupil

DR EVAN W THOMAS (by invitation) I cannot agree that dementia paralytica and tabes are meningovascular in the same sense Dementia paralytica is a meningoencephalitis The vessels are always involved, but there is always a decided atrophy of the parenchyma, and hordes of spirochetes are observed in the parenchyma of the brain No one has ever found spirochetes in the dorsal columns of the cord That indicates a difference Here is another interesting point If a man with clinically severe dementia paralytica is given malaria, he may recover Such cases have been described In an instance which I recall, a man functioned well and remained well for twenty years At autopsy the brain showed atrophy from the former injury of the brain and he could not have functioned with that brain without treatment There is no treatment like that for advanced tabes dorsalis, as far as I know

Postarsphenamine Jaundice Presented by DR NATHAN SOBEL

W K, a man aged 36, is presented from the Lower West Side Social Hygiene Clinic of the Department of Health The patient was previously presented before the Section of Dermatology and Syphilis in a symposium on syphilis on Feb 24, 1939 (ARCH DERMAT & SYPH 40 611 [Oct] 1939) Since that time the Wassermann reaction has been 3 plus, while at the previous presentation it was 1 plus After seven injections of arsphenamine (average dose, 0.3 Gm) symptoms of nausea and epigastric pressure developed Seven days after the last injection the patient showed marked icterus The urine gave a strongly positive reaction for bile The edge of the liver was palpable about 2 fingerbreadths below the costal margin but not tender Since then the patient has received three injections of sodium thiosulfate, 1 Gm per dose, and one injection of a bismuth preparation

DISCUSSION

DR LEO SPIEGEL This case of jaundice resulting from the administration of an arsenical is the first one of its kind that I have encountered in years I asked the patient whether he had been directed as to his dietary regimen before or after the arsenical was given He said that he was told not to eat anything for three hours prior to the injection and also after the injection Such directions are not in my method of procedure Some observers (Luke) have stated that a high carbohydrate diet increases the tolerance of the arsphenamines Craven said that a diet high in fat and protein provides maximum protection against injury to the liver from the arsenicals I instruct my patients to have a light breakfast, and I advise them to take some carbohydrate, usually milk chocolate, one-half hour before the injection of the arsenical I have not observed the development of jaundice in over six or seven years Arsenic has a predilection for the liver, and when carbohydrates are given before the injection the liver is filled with glycogen and thereby jaundice, which was customarily observed after the giving of arsenicals, is prevented

DR FRANK E CROSS (by invitation) In the past four years I have observed about 8 cases of jaundice, whereas before that time I do not remember having encountered a case in about six years I think the jaundice is probably due to the kind of arsphenamine used in treatment of these patients I believe the type of arsphenamine administered is an important factor as to whether or not jaundice will develop

DR E W ABRAMOWITZ Jaundice may develop in a syphilitic patient before arsphenamine is received as a result of either a syphilitic hepatitis or a nonspecific duodenitis (the latter may assume almost epidemic proportions) After the administration of arsphenamine jaundice may be due to an arsenical hepatitis, a Herxheimer reaction or a coincidental disease of the biliary tract On general principles, in case jaundice develops I stop the treatment with arsphenamine I have tried feeding patients sugar, I have been told to give them proteins and I have been told to starve them I think it is difficult to say what is best to do Let the jaundice subside and then begin treatment cautiously to see whether an arsenical can be tolerated later

DR NATHAN SOBEL In reference to what Dr Spiegel said, I usually tell the patients to take some carbohydrate one hour before the injection This patient apparently did not follow instructions Recently in the clinic 5 or 6 patients were seen within several weeks in whom jaundice developed, whereas previously no jaundice was seen for a considerable period According to the literature, it seems to be every one's experience that cases of jaundice are not observed for a while, and then a number of them appear The administration of arsphenamine to this man was stopped a few weeks ago, and a few injections of sodium thiosulfate were given, but he was also given a bismuth preparation because if antisiphilic treatment is stopped in these early conditions, acute syphilitic meningitis may develop After several months of treatment with bismuth preparations, in previous cases, small doses of arsphenamine were tried again In every case the patients were able to tolerate full arsphenamine treatment later However, if jaundice should develop again after the second attempt, that is a permanent contraindication for further arsenicals The initial Herxheimer reaction this man had was a reaction to the first injection of arsphenamine He never showed any further reaction after that The cause of jaundice in any individual case is not known, as Dr Abramowitz pointed out, as there may be many causes

Congenital Syphilis, Juvenile Dementia Paralytica, Interstitial Keratitis
Presented by DR LEO SPIEGEL

L D, a girl aged 18, presented from Bellevue Hospital, has congenital syphilis The diagnosis of juvenile dementia paralytica was first made in January 1935 From that time to August 1936 she received twenty-one injections of tryparsamide (2 Gm) and ten injections of a bismuth preparation In August 1936 the patient was admitted to Manhattan State Hospital for malarial therapy and underwent nine chills After the malarial treatment, she received thirty injections of a bismuth compound and twenty injections of neoarsphenamine (81 Gm)

In November 1937, while the patient was being treated a clouding of the left cornea developed, which was diagnosed as interstitial keratitis Treatment with neoarsphenamine and bismuth preparations was continued from that time throughout 1938 The keratitis improved slightly during this time In August 1938 a clouding of the right cornea was noted for the first time At this time she was receiving both bismuth subsalicylate (2 cc) and neoarsphenamine (0.45 Gm) each week, which treatment was continued to October 15, and then she was given mercury injections for six weeks At the end of her course of mercury injections, she was admitted to Bellevue Hospital From Dec 21, 1938, to the present time she has received twelve injections of arsphenamine (0.3 Gm each) and one injection of a bismuth preparation The keratitis has definitely improved but is not entirely healed as yet, according to the latest report from the ophthalmic clinic

At the Neurological Institute of New York in January 1936 the Wassermann reaction of the blood was 4 plus Examination of the spinal fluid showed the Wassermann reaction to be 4 plus in all dilutions, the cell count 5, the globulin content 1 plus, the total protein 58 mg per hundred cubic centimeters and the colloidal gold curve 5554332100 At Bellevue Hospital the Wassermann reaction of the blood on April 19, 1939 was 4 plus On Feb 1, 1939, the Wassermann reaction of the spinal fluid was 4 plus in all dilutions There were no cells or

globulin and the colloidal gold curve was 2211000000 A roentgenogram of the heart and the aorta on Dec 28, 1938 was normal

DISCUSSION

DR EVAN W THOMAS (by invitation) The case is presented chiefly because an interstitial keratitis developed after the patient had had malarial treatment The diagnosis of juvenile dementia paralytica was definite The condition was greatly benefited by the malarial therapy, but even with the decided improvement in mental and emotional symptoms the interstitial keratitis developed

DR FRANK E CROSS (by invitation) I think the condition in this case is malignant syphilis A varied program of therapy must be kept up, using different drugs and different types of arsphenamine (such as silver arsphenamine and possibly in this case acetarsone), along with large doses of iodides intravenously I should also recommend courses of mercury preparations and would treat the patients persistently without rest periods, in order to prevent complications

DR HERMAN GOODMAN Are all this patient's symptoms due to syphilis? There may be a patient with syphilis who shows symptoms which are not due to *Spirochaeta pallida* or who has a disease not caused by *S pallida* In former times, it is true, many clinical conditions were ascribed to syphilis Alopecia areata is still held by some foreign authors to be syphilitic Strangely, interstitial keratitis in the older books was taught to be possibly due to something other than syphilis May not the treatment given this patient be the cause of the clinical signs of interstitial keratitis, just as in the case presented by Dr Thomas the osseous lesions might have been due to the treatment rather than to the syphilis? Thus when the symptoms do not disappear more treatment is given, with the result that more symptoms occur, leading ultimately to symptoms which are nonsyphilitic and which are not helped by antisiphilitic therapy, which in turn causes further symptoms

DR EVAN W THOMAS (by invitation) I agree decidedly that etiologic factors other than syphilis ought to be looked for in the first case in which periostitis developed during treatment and in this case of interstitial keratitis I have asked the orthopedists what other than syphilis could cause periostitis and got no answer, but I agree it certainly should be considered One should not be absolutely dogmatic about saying that the condition is a syphilitic periostitis In the present case, there is a note on the chart by the ophthalmologist to the effect that he does not believe that the condition is an interstitial keratitis It is a deep process, similar to the interstitial keratitis of syphilis, but he advises looking for foci of infection I have looked Tuberculosis has been definitely ruled out Furthermore, the patient is getting better Maybe she would have recovered anyway She has better vision now in the left eye Until I can find some other cause, I am going to treat the disease that usually causes periostitis in the one case and the disease that usually causes interstitial keratitis in the other case

BROOKLYN DERMATOLOGICAL SOCIETY

MORTIMER J CANTOR, M D, *President*

SEYMOUR H SILVERS, M D, *Secretary*

April 17 and May 15, 1939

Senile Elastosis and Acrodermatitis Chronica Atrophicans Presented by
DR ABRAHAM WALZER

M C, a man aged 63, a carpenter, came to the dermatologic clinic of the Jewish Hospital about three weeks ago, complaining of an infection on the right cheek, pigmented patches on the face and neck and lesions on the lower extremities

As presented tonight, he shows a follicular infection of the right cheek which has improved considerably. The pigmented patches are on the back of the neck, about the eyebrows, on the skin adjacent to the inner canthus of each eye and on the helix and anthelix of each external ear. The color varies from ivory white (ears, eyebrow area) to yellow (neck). The white areas are smooth, soft, sharply outlined and not elevated or only faintly elevated. The patch on the neck feels thickened but soft, and the natural cutaneous folds are accentuated. There is no suggestion of a papule as the primary lesion, though there are a few scattered pigmented points (level with the skin) surrounding the patch on the neck.

On the posterior part of the hard palate and on the soft palate is a patch composed of tiny telangiectatic points on a yellow pigmented surface.

On the lower half of the trunk and on both lower extremities, extending to the toes, is an extensive diffuse atrophic dermatitis. All stages of this dermatitis can be seen, from bright red to dusky blue erythema and from raised, inflammatory boggy patches (lumbar region) to thin, wrinkled skin. The subcutaneous veins stand out prominently. The icteric index and the valves for total and free cholesterol and for sugar were within normal limits. The urine showed no abnormalities.

A section taken from the lesion on the neck showed atrophy of the epidermis with flattening and disappearance of the papillae. Immediately beneath this was a mass of degenerated elastic tissue extending across the section in a bandlike area. The elastic fibers were thickened, broken and twisted.

DISCUSSION

DR. M. L. WEITZ, Jamaica, N. Y. As far as the lesion on the right cheek is concerned, one must consider the possibility of basal cell epithelioma. Until a biopsy is done, however, I do not think a diagnosis can be made.

DR. JACOB SKEER. The location of the lesion along the neck and the color of the lesion fit in with the description of pseudoxanthoma elasticum. On the other hand, one of the diagnostic characteristics of that condition is that it does not occur at the sites of true xanthoma, and this man has lesions on the eyebrows, on the ears and on the soft palate. The histologic report should clarify the diagnosis. The retina should be examined for angioid streaks. I do not know exactly how to classify the yellowish infiltrated lesions on the eyebrows. They fit into the picture of any of the fatty degenerative processes.

DR. A. M. PERSKY. Clinically I think the diagnosis rests on the histologic study of tissue removed from lesions in various sites.

DR. DAVID M. DAVIDSON. Cutaneous changes like those on the patient's neck are seen in senile elastosis as well as in pseudoxanthoma elasticum. One must, however, admit that the changes on the neck, eyebrows and palate are the same and are expressions of the same condition. Pseudoxanthoma elasticum does not occur on the face, senile elastosis does. The age of the patient is in favor of the diagnosis of senile elastosis. The pathologic changes are similar in these two diseases and a differential diagnosis based on pathologic study alone is difficult, although the elastic tissue is said to be more superficially located in senile elastosis.

DR. ABRAHAM WALZER. Senile elastosis means senile changes in the skin occurring usually after the age of 40 years. Pseudoxanthoma elasticum, on the other hand, is invariably a disease of the young adult. Senile changes in the skin occur in two main forms. One is simple thinning and wrinkling, producing transparency, so that the cutaneous vessels can be seen. In the other type, as in this case, there is thickening of the skin, which usually implies senile atrophy plus external exposure to changeable weather. This type occurs in seamen, peddlers and other persons excessively exposed to the elements. This patient is a carpenter, but most of his work is outdoors.

As to the histopathologic picture, it is true that senile elastosis and pseudoxanthoma may show similar pictures. Nevertheless, pathologic study in conjunction with the clinical picture usually makes it possible to differentiate the two.

conditions Atrophy of the epidermis and elastic changes high in the section of skin speak more for senile elastosis than for pseudoxanthoma elasticum

Against pseudoxanthoma elasticum, therefore, are the following points the age of the patient, the lesions on the face, the color of the facial patches, the absence of primary papules, the histologic picture of epidermal atrophy and the characteristic layer of degenerated elastic tissue high in the section, directly beneath the basal layer

The lesion on the cheek is a simple infection which is rapidly subsiding

There is nothing I can say about the acrodermatitis atrophicans except that it is rather extensive Its association with senile keratoses is interesting because of a common elastic tissue disturbance

Schamberg's Disease (Unilateral) Presented by DR L FRUCHTBAUM

P F, a girl aged 9 years, was seen at the Lutheran Hospital in January 1939, complaining of an eruption on the left forearm, of nine months' duration The flexor surface of the left forearm was covered with patchy lesions of varying sizes There were reddish and purplish elements within the patches, giving the appearance of purpura Of late the lesions have become paler and the redness has disappeared, and at present the lesions have diminished and have assumed a brownish tint A blood count showed 3,760,000 red cells per cubic millimeter, with 67 per cent hemoglobin, and 3,550 white cells per cubic millimeter, with a differential count of polymorphonuclears 45 per cent, lymphocytes 48 per cent, eosinophils 2 per cent and macrocytes 5 per cent The bleeding time was one minute and fifty seconds The coagulation time was five minutes and ten seconds The platelet count was 206,800 The Wassermann and Kahn reactions were negative A roentgenogram of the cervical part of the spine taken to ascertain whether cervical rib was present failed to reveal that anomaly

DISCUSSION

DR ABRAHAM WALZER I cannot see why this case is presented as an instance of Schamberg's disease There is no resemblance to that condition My impression is that the eruption is either linear lichen planus that is fading or a linear nevus I think that histologic examination of a piece of tissue would help considerably in the diagnosis

DR MORRIS M ESTRIN If the eruptions were located on both lower extremities with a history of progression with redness and with final fading into yellowish brown lesions, I should consider Schamberg's disease, but the fact that the eruption is on the upper extremity makes me disagree with that diagnosis, in spite of the fact that the condition followed involvement of the lower extremities It may be fading lichen planus or a nevus, or possibly it is some hemorrhagic disturbance, trauma or old herpes zoster I should not consider a diagnosis of Schamberg's disease

DR JACOB SKEER I think that probably a pigmentary analysis of the lesions would be enlightening In other words, a Perl test should be done to find out whether iron pigmentation is present If the results were positive, it would probably indicate some pigmentary disturbance If the dopa reaction were positive, the melanin would cause one to consider pigmented nevus I have never seen Schamberg's disease of this type Schamberg's disease is known to be a disturbance which does not fade but progresses to atrophy, with purpuric puncta, telangiectasia and pigmentation Even Majocchi's disease cannot be considered in this case In my opinion, the condition is either a chronic lichenoid pigmentary disturbance or the remains of an inflammatory process

DR DAVID M DAVIDSON There is an active lesion on the dorsum of the little finger which is slightly elevated and purplish Were the lesions on the forearm the same originally? Early lesions of Schamberg's disease do not have this appearance

DR SEYMOUR H SILVERS I should like to mention a case which has been under my observation for the past two months, that of a young woman who presents lesions identical with those of this patient. Along the ulnar surface of the left upper extremity there are patches of various shades and colors. The eruption started as typical linear lichen planus nine months ago, and the pigmentation has remained.

DR L FRUCHTBAUM Three or four diagnoses have been offered for consideration. A postinflammatory process has been suggested. During the past three months there has been no evidence of inflammation. The patient has never complained of itching, pain or other disturbance. As for lichen planus, there have at no time been any papules resembling it, and there is no evidence that the process has been going down to depigmentation as a residue. There are now new lesions. This has been going on for the past three months. Some of the old lesions have faded, and a new crop has appeared. The lesions merge to form a patch and create various colors—deep blue, purple and red. If the condition were nevus, the process would be stationary. As to urticaria pigmentosa, there is no inflammation or itching, and the general appearance of the lesions is not that of urticaria pigmentosa. Several months ago I presented a patient with similar lesions, but on the lower extremities. My impression of this case is that it is an unusual one of Schamberg's disease.

Tabes (Charcot Knee, Atrophy of the Optic Nerve, Chorioretinitis)

Presented by DR ABRAHAM WALZER

C F, a woman aged 49, married but never pregnant, came to the clinic of the Jewish Hospital because of inability to bear weight on her left knee. There was no history of any previous illness or of any primary or secondary manifestations of syphilis. In 1935, one year before her appearance at the clinic, she had been in an accident, after which her left knee became painful and swollen. The Wassermann reaction in 1936 was negative.

Examination at present reveals pupils that do not react to light but do react in accommodation. The left fundus shows atrophy of the optic nerve, and the right, diffuse chorioretinitis. The knee and ankle jerks are absent. The Romberg test gave a positive result. The finger to nose test shows ataxia. The gait is ataxic and spastic. The sense of position of the toes is impaired. The vibratory sense is impaired. The heart and lungs are normal.

In 1936 the Wassermann reaction of the blood was negative, but that of the spinal fluid was 2 plus. Examination of the spinal fluid disclosed no cells, a negative reaction for globulin, a value for total protein of 23 mg per hundred centimeters and a colloidal gold curve of 22222000000. In 1937 another examination showed the Wassermann reaction to be 4 plus, the reaction for globulin was negative, there were no cells, and the colloidal gold curve was 4422211110.

A roentgenogram of the left knee showed advanced hypertrophic changes with increased density of the articulating and adjacent portions of the joint. The joint body presents calcification and ossification of the medial lemniscus (Charcot joint with osteoarthritis).

The results of treatment were unsatisfactory, because of the patient's irregular attendance at the clinic.

DISCUSSION

(The diagnosis was accepted.)

Recurrent Cellulitis Resulting in Chronic Lymphedema Presented by DR A M PERSKY

R S, a Negro aged 29, was admitted to the King's County Hospital on March 27, 1939, complaining of pain, malaise, anorexia, fever and swelling of the right leg of several days' duration. He had had a number of similar attacks, involving both legs, from the age of 8 years until four years ago, when he came

to New York from North Carolina. The attacks usually appeared in the spring, and recovery was apparently complete in several days. He had had no attacks since coming to New York, but three years ago he had an "operation" for an enlarged inguinal gland.

Examination showed an acutely ill patient with a temperature of 102 F. The condition of the right leg appeared like acute cellulitis with deep thrombophlebitis. With rest in bed, local wet dressings and administration of sulfanilamide by mouth, recovery ensued in ten days. Roentgenograms of the legs were normal. The patient now shows decidedly stretched skin on the legs, hanging in folds over the infiltrated subcutaneous tissue. There are no enlarged inguinal glands.

DISCUSSION

DR SEYMOUR H. SILVERS: The skin on one of the legs is relaxed, but I am sure that this is not a case of cutis laxa, or Ehlers-Danlos syndrome, for none of the classic signs of this syndrome are present. This man had elephantiasis of both legs, of unknown cause. Three years ago I studied two brothers and their father who had conditions similar to that shown by this patient. They had Milroy's disease, which is familial. I questioned the patient in the present case, and he gave no familial history of this condition or anything similar to it. Nevertheless, I am inclined to think that this case fits into the picture of Milroy's disease. The other two boys had attacks similar to those which this patient described. There were sudden attacks of swelling which looked like erysipelas or cellulitis, accompanied by high temperature and extreme pain. These attacks would occur as often as once in three months. Various studies were made, but no etiologic factor could be determined.

DR. L. FRUCHTBAUM: During the past few years I have observed several such cases of lymphedema, and in all of them the condition started like erysipelas. The patient in this case is a Negro, and therefore one could not see the characteristics of erysipelas. Examination of the toes of this patient reveals a classic picture of dermatophytosis. This I have noticed also in my own cases. I think more attention should be paid to infections between the toes in order to check a recurrence of the attacks.

Unilateral Acrocyanosis Presented by DR. L. FRUCHTBAUM

S. G., a woman aged 34, was seen at the Lutheran Hospital on March 16, 1939, complaining of swelling and discoloration of the left hand and fingers for the past year. There are definite swelling and dark bluish discoloration of the left hand and fingers, particularly on the dorsum of the hand. There is increased sensitivity to touch of the left hand. There is no pain or itching. The left hand feels cold. There is no blanching on raising of the left arm.

On examination the blood pressure and the pulse were equal on the two sides, the blood pressure was 175 systolic and 100 diastolic. The Wassermann reaction of the blood was negative. The urine was normal. The basal metabolic rate was +7 per cent. A roentgenogram of the cervical portion of the spine did not reveal cervical rib. A roentgenogram of the left hand showed hypertrophy of the joints.

DISCUSSION

DR. DAVID M. DAVIDSON: Besides the cyanosis there are definite atrophy and wrinkling of the skin, and I consider this case one of acrodermatitis chronica atrophicans. It presents two rare and interesting features, the unilateral distribution and the osseous changes.

DR. C. THOMAS CHIARAMONTE: I wish to mention the fact that between the third and the fourth finger there is pronounced erosio blastomycetica.

DR. L. FRUCHTBAUM: I presented this case to rule out the presence of cervical rib in a unilateral cutaneous lesion. One seldom sees acrocyanosis on one side of the body only. The patient complains of nothing but loss of sensation.

in the hand The roentgenogram of the hand shows no arthritis but reveals hypertrophy and a large number of blood vessels Obviously there is some obstruction to circulation of the blood in the hand which causes the present condition

1. Late Secondary Syphiloderm 2 Syphilitic Osteitis? Presented by DR M DICKMAN

A W, a Negro aged 48, is presented from the Jewish Hospital The patient states that he had a chancre about twenty years ago In 1927 he complained of abdominal pains and because of a positive Wassermann reaction received six injections of neoarsphenamine and six of a bismuth compound, with improvement in his symptoms In 1930 he went to the Department of Health Clinic because of abdominal pains and received treatment for two years During this time his symptoms were relieved In 1933 they returned In 1934 he received six months' treatment by a private physician From May 1938 to February 1939 he received twenty injections of a bismuth compound and twenty of neoarsphenamine at the Jewish Hospital

He presents a single annular lesion the size of a silver dollar in the episternal notch The border of the lesion is composed of edematous erythematous papules, the center being hyperpigmented

This lesion developed in February 1939 and has increased to its present size in spite of five injections of a mercury compound and five of a bismuth compound In June 1938 there were three similar annular lesions, two on the left side of the chest and one on the right arm These lesions disappeared in about two weeks under arsenical therapy Histologic examination at that time showed dense collars of plasma cells about the blood vessels, and a pathologic diagnosis of a secondary syphiloderm was made

A roentgenogram of the pelvis taken in April 1938 showed decided increase of osseous density of the entire left half of the pelvic girdle, the most pronounced condensation appearing in the region of the lower part of the ilium and the ischial bones In the ischial and pubic bones there were small irregular areas of lessened density

DISCUSSION

DR. DAVID M. DAVIDSON A few months ago this patient presented a lesion on his chest similar in outline and consistency to the lesion now present on his neck At that time I was doubtful about the syphilitic origin of the lesion, because of its edematous appearance and consistency, pathologic study of the lesion, however, proved it to be a secondary syphiloderm, and it promptly disappeared under arsphenamine therapy The present lesion appeared while the patient was receiving injections of a bismuth compound and does not regress, although this treatment is continued This patient is probably bismuth resistant, and the lesion will disappear as soon as he again receives arsphenamine therapy

DR M DICKMAN The lesion on the neck must be accepted as a late secondary syphiloderm because of the characteristic pathologic picture The involvement of the left innominate bone was considered as a possible manifestation of Paget's disease or as a metastatic process from a malignant process of the thyroid or of the prostate As these conditions were excluded by careful study, one must, by exclusion, consider this process a syphilitic osteitis

A Case for Diagnosis (Bowen's Disease? Superficial Epithelioma?) Presented by DR M DICKMAN

R T, a woman aged 75, is presented from the Jewish Hospital She shows a single arciform flat erythematous patch the size of a silver dollar on the left side of the sacral region of the back There are many hard, yellowish crusts on the surface, especially at the edges Slight atrophy is present in the center of the lesion

This lesion appeared about six years ago and has increased slowly in size. The patient complains of moderate itching of the patch. Topical applications are the only treatment she has received in the past two years.

DISCUSSION

DR ABRAHAM WALZER It is difficult to make a diagnosis of Bowen's disease clinically, for that reason either an epithelioma or Bowen's disease was suggested. I should like to know about the therapy in this particular case.

DR L. FRUCHTBAUM I do not think the condition requires any therapy.

DR A. M. PERSKY I should either use wide electrodesiccation (about $\frac{1}{2}$ inch [1.3 cm] beyond the margin) or excise the lesion.

DR JACOB SKEER I have found that such lesions respond poorly to roentgen and radium therapy. Probably desiccation is the method of choice.

DR M. L. WEITZ, Jamaica, N. Y. I feel as Dr Fruchtbaum does regarding therapy in a case like this. I think the lesion should be left alone. The patient is old, and the lesion has been present for five or six years. It is not causing any discomfort or pain.

DR MORTIMER J. CANTOR This is a case of Bowen's disease, which should never be left alone. The lesion should be desiccated and curetted completely.

DR M. DICKMAN Material for a biopsy was taken, and the histopathologic report was epithelioma in Bowen's disease. In this case I believe that excision of the entire lesion is the treatment of choice.

Multiple Superficial Epitheliomatosis Presented by DR H. L. FEIGENBAUM

M. H., a widow aged 65, born in the United States, states that her present lesions started fifteen years ago, at which time several small reddish areas appeared on the forehead and cheeks. These developed slowly, and nine years ago a small (cystic?) lesion developed on the right cheek. This was removed with radium. Similar but flatter lesions developed on the forehead and other parts of the face. These were treated with twenty to thirty applications of the roentgen rays. Itching was present at times. The past history was irrelevant.

The patient presents multiple yellowish red macular and flat papular lesions on the forehead and cheeks varying in size from that of a split pea to that of a lentil and slightly larger. Some have coalesced by peripheral extension to form irregular, larger patches. Scaling is present in practically all. In the center of the forehead there is a large patch showing crusting, which has been traumatized by scratching. The right cheek presents a white scar at the site of the removed cyst (?) nine years ago. In addition, there are several patches of senile keratosis. The dorsa of the hands present several superficial erythematous lesions similar to those on the face.

Lupus Vulgaris Presented by DR JACOB SKEER

J. M., a man aged 61, born in Poland, came to the Israel-Zion Hospital complaining of an eruption on the face of twenty years' duration.

The patient has had hay fever for five years and had pneumonia in 1937.

Examination shows an irregular circular lesion the size of a half-dollar in the left temporal region, crossing the outer half of the eyebrow and the upper lid and completing the circle on the temple. The margin is made up of firm, red-brown nodules the size of millet seeds and about three or four deep. Some of the nodules are crusted, and diascopic pressure shows the apple jelly color. The center is slightly edematous and covered with fine scales, but no nodules can be seen. An oval similar patch is present on the left side of the lower jaw, near the chin.

A roentgenogram showed clouding of the apexes of both lungs but no active process.

The histologic diagnosis was lupus vulgaris.

DISCUSSION

DR C THOMAS CHIARAMONTE I agree with the diagnosis as presented I feel that a diet free of salt is of value in such a case

DR L FRUCHTBAUM I cannot suggest any therapy that has been successful in my own experiences

DR ABRAHAM WALZER This is a type of lupus vulgaris, but I think it belongs to the Leloir type of lupus erythematosus From the first glance at this patient lupus vulgaris would never enter any one's mind There is a definite appearance of atrophy, and the lesion looks erythematous

DR MORTIMER J CANTOR I think a condition like this would do well with ultraviolet irradiation with a water-cooled quartz mercury vapor arc lamp, the exposure starting with thirty seconds and increasing to sixty or eighty seconds once a week, with pressure for ten or twelve treatments I have seen improvement from this treatment in a number of cases The treatment should be given to the cheek and forehead and not to the eyelid

A Case for Diagnosis (Eruption Resembling Granuloma Annulare) Presented by DR JACOB SKEER

D T, a boy aged 7, born in the United States, was brought to the Cumberland Hospital complaining of an eruption of two years' duration

The patient had measles, pertussis, chickenpox and "running ears" as an infant He had a "heat rash" when he was 2 years old The mother stated that he had head colds frequently

The mother has lichen planus

The eruption seen in the boy is varied and polymorphous and is described as grouped, discrete pinhead-sized papules on the anterior and lateral aspects of the neck Several erythematous lesions with ringed papular margins are distributed on the arms, forearms, thighs and legs A large patch (5 by 6 cm), mildly erythematous and made up of pinhead-sized conical papules and atrophic spots, is situated on the chest, below the ensiform cartilage and the margin of the ribs A similar patch is situated over the dorsal portion of the spine, and there are several smaller lesions on the back and the abdomen

The condition began on the outer aspect of the left ankle, which now presents an irregular rectangular area, sharply defined and slightly hyperkeratotic

The reaction to tuberculin was negative with dilutions of 1 1,000,000, 1 100,000 and 1 10,000

A roentgenogram of the chest showed the shadows of both hili to be accentuated, with several small calcific deposits and accentuation of the inferior root, trunk and branches

DISCUSSION

DR DAVID M DAVIDSON If I had not seen the lesions on the body but had looked at only those on the extremities, I should not hesitate to make a diagnosis of granuloma annulare I cannot make up my mind as to the lesions on the trunk The patches show distinct papules at their peripheries, but the papules are much smaller than those usually seen in granuloma annulare I am unable, however, to suggest any other diagnosis

DR L FRUCHTBAUM I do not think one is justified in making a diagnosis of this lesion without a biopsy The early lesions are nodules The eruption probably is a form of cutaneous tuberculosis

DR ABRAHAM WALZER All the lesions on the body are of one type They are scattered over the trunk and extremities and are tiny papular lesions that disappear under pressure They have a tendency to grouping, eventually they form a small ring or groups, as on the forearm, and then progress further, producing larger rings and patches I think the whole process is one I confess I cannot exactly classify this condition with any entity that I know of, but I wonder

whether it does not fit into the group of dermatoses described under the head of annular erythemas of Lipshutz or Darier. However, I think this condition is an acute inflammatory process and not granuloma annulare.

DR DAVID M. DAVIDSON: Perhaps I did not make myself clear. I did not mean that the patient presents two conditions. I stated that I have not seen granuloma annulare produce such lesions as those on the trunk of this patient, but I consider them part of the same process as those on the extremities.

DR C. THOMAS CHIARAMONTE: I observed a case about one month ago in which the patient had a lesion similar to the one on this patient's left ankle. It was a wide plaque with a typical raised granulomatous border that was smooth all around, and the center was dotted with pinhead nodules which had become pigmented. The biopsy specimen was reported as representing granuloma annulare. This may be an unusual type of that disease.

A Case for Diagnosis (Moniliasis?). Presented by DR. MORTIMER J. CANTOR

M. S., a married white woman aged 31, was first seen on May 11, 1939, at the Beth Moses Hospital Dispensary. The past history was of no importance.

The first eruption dates back three years, when the patient noticed three small spots, one on the right cheek, one on the left breast and one on the flexor surface of the forearm. Within three months the eruption became widespread, covering the upper and lower extremities and the torso in irregular patches of papulovesicular oozing dermatitis. She was treated with various salves and lotions irregularly at other institutions for a year and a half, with little improvement. She then went to a private physician, who "cleared up the condition with diet, internal medicines and salves," leaving pigmented spots. The patient remained free from lesions for about six months.

The present eruption began about September 1938, with moist, elevated, infiltrated patches on both areolas, and spread to its present extent. Little treatment was given until April 1939, when four roentgen treatments were administered to both breasts, one each week, the last one having been given about May 1, with practically no effect on the eruption.

The patient is normally developed. The upper and lower extremities have variously sized circinate and spotty patches of variegated brown discolorations covered with fine furfuraceous scaling; these are the remains of the original eruption. There are no signs of pruritus.

On both breasts, mainly about the areolas but also involving the glabrous skin, are many papulovesicles ranging in size from that of a large pinhead to that of a lentil, some being considerably more elevated than others. Many of the flatter ones are red and exceedingly moist. The latter type makes up the majority of the individual lesions. The patches, which are mostly confined to the areolas and especially to the left side, vary from the size of a pea to about that of a silver quarter and are composed of the flat-topped, drier papules. The color of these papules varies from brownish red to yellowish brown, and many, especially the moist ones, are covered with a yellow-brown, sanguineous impetiginous crusting. The patches are considerably elevated, fungoid and papillomatous.

The patient's tongue is moist and is irregularly furrowed throughout its extent with areas of hyperkeratosis and depressions which give the appearance of being denuded of epithelium.

The laboratory reports were as follows. The Wassermann reaction was negative. The urine was normal. Cultures of material taken from the tongue and from the lesions have not yet been reported on. The result of the oidiomycin test was positive. A direct smear of material from the tongue showed a network of branching and filamentous hyphae and yeastlike organisms (*Oidium albicans*). A direct smear of material from the lesions on the breast was negative for *Monilia* or hyphae. A biopsy specimen taken on May 11 showed nothing characteristic. A tuberculin test done on May 27 with a dilution of 1:10,000 gave a negative result.

DISCUSSION

DR. L. FRUCHTBAUM I think the patient has had too much medication. She is of a neurotic type. I suggest the use of mild topical applications.

DR. SAMUEL HECHT All I could make out was a dermatitis, and ordinarily I should have no doubt of its parasitic nature. Formerly it was called just eczema.

DR. ABRAHAM WALZER I saw this patient a couple of years ago. At that time she had a fairly generalized eruption involving not only the areas now affected but the upper extremities and even the thighs and the lower part of the abdomen. The condition was diagnosed as some type of parasitic infection, and she was treated accordingly. The condition cleared up almost completely but broke out again. Finally the patient disappeared. She came to the Beth Moses Clinic a few days ago with the present eruption. As to the question of moniliasis, I think it is not going to be an easy matter to prove whether this is true moniliasis of the skin. If the same monilia could be obtained from the intestinal tract, from the mouth and from the lesions it would be strong evidence in favor of such a diagnosis.

Keratosi s Pilaris. Presented by DR. MORRIS M. ESTRIN

M. M., a white man aged 69, was referred to the dermatologic department of the Kings County Hospital on account of a peculiar eruption on the skin, resembling pediculosis pubis.

The past history was irrelevant except for a long history of urticaria and pruritis.

About two years ago the patient noticed pigmented papular lesions on the hairy portion of the body. They never caused him any concern except for occasional itching.

Examination reveals that on the arms, legs, chest, back, hips and upper parts of the thighs there are soft horny papules, situated around the pilosebaceous orifices. On removal of these horny plugs, a coiled hair can be seen, embedded in the sebaceous deposit in the follicle.

DISCUSSION

DR. SEYMOUR H. SILVERS I wonder whether a biopsy of material from a hair follicle would provide a clue to the reason for the peculiar coiling of the hair. There must be some cause for the peculiar shape assumed by the hair.

DR. L. FRUCHTBAUM I recently gave viosterol to a patient with keratosi s pilaris and obtained remarkable response, so perhaps this condition is due to avitaminosis.

DR. MORRIS M. ESTRIN I asked the man about his diet. He is peculiar in this respect. He does not like fish, milk, eggs or meat. Nothing smells right to him. He has trouble with his nose. He has had complaints for the last two or three years. Perhaps with a new diet and vitamin A it will be possible to improve his general condition and his skin.

A Case for Diagnosis (Dermatitis Venenata?). Presented by DR. SEYMOUR H. SILVERS

J. K., a married man aged 34, a physical therapist, complained of an eruption of the face and forehead of two years' duration. The eruption has changed in intensity during this period, and one year ago, while the patient was visiting in Syracuse, N. Y., the eruption cleared entirely. The patient had received various topical treatments, injections of a gold compound, roentgen therapy and various medications administered orally. Improvement has been noticed lately with roentgen therapy, a mild cream for the face and intravenous administration of calcium gluconate. The following diagnoses have been considered: lupus erythematosus, rosacea, seborrheic eczema, psoriasis and contact dermatitis. In the past

ten days a follicular papular and vesicular eruption has appeared on the upper extremities and it has now spread to the upper part of the trunk. The eruption has not been especially itchy.

The urine was normal, and the Wassermann reaction of the blood, negative. Roentgen examination of the sinuses showed them to be normal. Attempts were made to eliminate known irritants in the home.

Examination now shows swelling of the face and eyelids. The skin of the face and forehead is covered with a patchy eruption of vesiculopapular and somewhat crusted lesions. There are some patches, ranging in size from that of a dime to that of a quarter, on the sides of the face. There are some scaling and redness back of the ears. Mainly on the flexor surface of the upper extremities and on the trunk there are numerous scattered and well defined patches of pinhead-sized to dime-sized crusted and scaly follicular papular lesions. The scalp is clear, and there is an abundant growth of hair. On the sternum there is a well defined quarter-sized reddish yellow scaly lesion.

DISCUSSION

DR MORRIS M. ESTRIN The patient stated that the onset was due to sunburn originally contracted a few years ago. He is a physical therapist, with the use of plenty of apparatus. How much treatment he has given himself I do not know. I think this condition belongs to the lupus erythematosus group.

DR L. FRUCHTBAUM I shall venture the diagnosis of some type of tuberculosis, perhaps Lewandowsky's rosacea-like tuberculid.

DR SAMUEL HECHT From the appearance of the lesions I agree with the presenter's suggested diagnosis of dermatitis venenata, and I have no doubt that the patient has been using something besides what the physician prescribed for him. When the dermatitis venenata clears up, perhaps it will be possible to tell what the underlying condition was.

The fact that the patient is a physical therapist and is perhaps using some treatment without mentioning it must be considered.

DR JACOB SKEER I should like to venture a diagnosis of the Senear-Usher type of lupus erythematosus. The lesions on the back appear pemphigoid.

Von Recklinghausen's Disease Presented by DR JACOB SKEER

M. R., a married woman aged 52, born in Poland, came to the dermatologic clinic of the Jewish Hospital, complaining of numerous tumors on the body.

The past history was irrelevant.

Examination shows numerous tumor-like lesions varying in size from that of a small pea to that of a hazelnut, distributed on the face, trunk and upper and lower limbs. The lesions are soft and sessile, becoming easily invaginated on pressure. Some of the lesions are the color of normal skin, others have a bluish tinge. There are several vascular nevi, as well as generalized freckling and larger and variously shaped cafe-au-lait patches.

DISCUSSION

(The diagnosis was accepted.)

A Case for Diagnosis (Lichen Planus Sclerosus et Atrophicus [Halo-peau])? Presented by DR MORRIS M. ESTRIN

M. R., a white man aged 50, is presented from the Kings County Hospital. He stated that a small papule developed on the dorsum of the left foot twenty-one years ago, while he was in the trenches during the war. The lesion grew slowly, showing activity at the border and turning white and atrophic in the center, until it reached its present size. Other lesions developed subsequently on the right foot and left hand.

The patient presents a sharply outlined palm-sized plaque on the dorsum of the left foot, with an atrophic center and a papular border. There is a coin-sized area at one corner of the lesion which is elevated and sclerotic. There are similar coin-sized lesions on the dorsum of the right foot and the dorsum of the left hand. There is a hard papule at the tip of the coccyx, with no atrophy.

Treatment for the past two weeks has been with boric acid ointment U S P. This has resulted in softening of the lesion.

DISCUSSION

DR ABRAHAM WALZER. Every time a case of this kind is presented the question of scleroderma, white spot disease and lichen planus atrophicus is brought up. To permit a diagnosis of lichen planus atrophicus, a papule of lichen planus must be seen. All such conditions can be put into three groups: those that begin as a lichen papule and end in atrophy, those that begin as white spots and end in atrophy, and those that are a cross between these two, that is, those that begin as lichenoid papules and end in atrophy. In this particular case all one sees are patches of atrophy with hyperpigmented borders. There is not the slightest evidence of lichen or a lichenoid papule. The condition belongs to the white spot or scleroderma group rather than to the lichen group.

DR SEYMOUR H. SILVERS. I do not think this is Csillag's disease. I saw this patient previously, and I suggested the diagnosis of lichen sclerosus et atrophicus. There was a great deal of discussion whether lichen sclerosus et atrophicus is a disease sui generis or whether it is related to the lichen group or to the morphea group. I think that any one may maintain either point of view and will find a sufficient number of articles to back him up. Miescher published an article (Miescher, G. Weissfleckenkrankheit [Lichen sclerosus—white spot disease—karten blattähnliche Skleroderma], Arch f Dermat u Syph 171 419-429, 1935) suggesting that this particular type of lesion belongs neither in the lichen group nor in the morphea group. It is a special disease that he called lichen sclerosus et atrophicus. However, this is not universally accepted. Miescher pointed out that in that type scattered lesions are found and some of them fit very well into the morphea-like group. Even the pathologic picture varies a great deal, some believe it fits into the lichen group and some believe it fits into the morphea group.

PHILADELPHIA DERMATOLOGICAL SOCIETY

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May 19, 1939

Virus Infection Resembling Herpes Simplex Presented by DR CARMEN CHRISTINE THOMAS, Wilmington, Del (by invitation)

L. R., a Negress aged 26, well nourished and well developed, presents hypertrichosis of the face and chin. She has had recurrent attacks of grouped vesicles in crops every two or three weeks for the past ten years. These lesions result in scar formation after ten or fifteen days. There are scars of former lesions on the back, abdomen, buttocks and thighs and active herpetiform lesions at some of these sites. The patient has latent syphilis of unknown duration, for which she has received since Sept 2, 1936, five injections of trisodium arsphenamine sulfonate and twenty-six of a bismuth compound. She had exfoliative dermatitis lasting five months in 1936 and acute pelvic inflammatory disease in 1938. Material from

a five day old herpetic lesion on the left knee was inoculated into the left cornea of a rabbit by scarification with a lancet. The right eye was scarified with a sterile lancet in the same fashion. Six days after inoculation the left eye began to exude creamy pus, and ten days after inoculation a pannus covered the entire left cornea. The right cornea remained normal. At this time (on the eleventh day) the animal became restless, the head was held flexed to the left and the right front leg became paralyzed (typical symptoms of herpetic keratitis and encephalitis).

DISCUSSION

DR ROBERT L. GILMAN: Why may not this condition be herpes simplex?

DR ELMER R. GROSS, Wilmington, Del.: I do not think that the lesions prove or disprove anything, because after injection one sometimes finds a traumatic reaction of the eye with leukoma as the result. I encountered this in experiments on interstitial keratitis.

DR ERICH URBACH (by invitation): I should like to commend Dr. Thomas because she was careful to perform a control test on the other eye. One eye was only scarified, and the other was scarified and inoculated. Only the eye which was inoculated is infected and shows keratitis. Encephalitis and paralysis cannot occur without infection. Dr. Thomas has in mind the possibility of desensitization. Hruszek suggested the possibility of immunizing persons with herpes simplex. He suggested the method of Pasteur, that is, to dry the brain and the spinal cord of an infected rabbit and to inject the prepared material in increasing quantities into the skin. I have tried the same procedure in cases of pemphigus. I have dried the brain and spinal cord from an animal infected with rabies and have injected this. The difficulty is that one always tries immunization too late. Animals seem to be easily immunized, but human beings are immunized only with great difficulty. I feel, however, that the immunization experiment should be performed in this particular case.

Imbibitio Lipoidica Collagendi Degeneratio Cutis Presented by DR. ERICH URBACH (by invitation) and DR. W. R. HILL (by invitation)

V. W., a white woman aged 52, presents at the external lateral surfaces of the arms, thighs and legs about a dozen indurated lesions of diversified appearance. The youngest lesion (three years old, on the external aspect of the left tibia) is about 4 mm in diameter, elevated, hard and reddish brown. The other lesions, varying in duration from ten to thirty years, are of three types. All are definitely located in the deeper parts of the cutis, the skin over them is depressed and violet-brown, they have a cartilaginous feel. Other lesions, also situated deep in the cutis, have an elevated, keloid-like surface. Two lesions (above the right anterior iliac spine and on the left thigh) differ from all the others in that they are yellowish brown but on pressure become distinctly yellow. Clinically, these lesions resemble necrobiosis lipoidica diabetorum. The patient had rheumatism at the age of 13, since then she has had five attacks about five years apart. The attacks have been limited as a rule to one joint, which has become red and swollen and required rest in bed for one month for relief. A tonsillectomy was done nineteen years ago. The first lesion (on the left hip) appeared thirty years ago, apparently associated with the rheumatic attack. The other lesions appeared on the arms, legs and thighs at various intervals, usually about five years apart, the last three years ago. None of the later lesions seems to have been related to the rheumatic infection. There is no history of preceding trauma. The value for total blood cholesterol was 363 mg, that for cholesterol esters 227 mg and that for free serum cholesterol 135 mg per hundred cubic centimeters. The sugar tolerance test gave a normal result. The blood serologic reaction of the blood for syphilis was negative. Histologic examination showed hyperkeratosis, there was abundant formation of connective tissue cells with deeply stained nuclei. The fibrils between them were condensed but contained spaces suggesting lipid sub-

stances, which were extracted with alcohol. Other parts showed fewer new connective tissue cells, but the fibrillar tissue appeared altered (basophilic degeneration of the collagen). The small vessels had thickened walls, and the cells of the intima were swollen. The Weigert stain revealed almost complete absence of elastic tissue. The sudan IV stain showed abundant brown-red globules and granules between the fibrils of the connective tissue and rarely in the cytoplasm. There were no foam cells. The fat was soluble in ether, partly soluble in alcohol and acetone and insoluble in chloroform. Doubly refractive bodies, fatty acids, soaps and amyloid were not demonstrable by suitable methods.

DISCUSSION

DR ERICH URBACH (by invitation). Two kinds of lipoidoses of the skin are now distinguished, the generalized and the localized. The three types of generalized lipoidoses are (1) xanthelasma, (2) extracellular cholesterinosis and (3) lipoid-proteinosis. Among the localized lipoidoses are recognized necrobiosis lipoidica diabetorum and the cutaneous lesions which are known as "sailor's skin," which are seen in old persons exposed for a long time to the sun and wind. The histologic studies presented suggest a type of lipoidosis which I have never seen before. It shows lipoid imbibition of the degenerated connective tissue.

A Case for Diagnosis. Presented by DR JOHN H STOKES

H B, a white man aged 32, presents a slightly raised, milky white, sharply demarcated plaque of irregular outline on the glans penis, on either side of the frenum and surrounding the meatus. There is a similar lesion on the under side of the foreskin. There is no inguinal adenopathy. In 1932 the patient noticed a minute white deep-seated papule in the glans penis, just adjacent to the meatus. This disappeared spontaneously in one year. In 1937 he noted a small, slightly elevated, somewhat shriveled white lesion on the glans penis, on both sides of the frenum, during the past year it has extended. There has never been any elevation or discharge.

DISCUSSION

DR THOMAS BUTTERWORTH, Reading, Pa. I think this man has balanitis xerotica obliterans, although there is no obliteration of the urinary meatus. The lesion has the same whitish, slightly depressed appearance as had that in a case I presented before this society (ARCH DERMAT & SYPH 35:1162 [June] 1937).

DR ERICH URBACH (by invitation). I agree with Dr Butterworth's diagnosis.

DR JOHN H STOKES. I have seen lichen sclerosus and lichen planus on the penis produce a picture something like this. I confess I lean toward the diagnosis of lichen sclerosus. I have not seen the other condition, so that I am not able to say whether I concur in that diagnosis. The original diagnosis made by one of my associates who saw the process a number of years ago, when it first began, was kraurosis occurring on the penis and equivalent to kraurosis vulvae in women. Ormsby stated that such a condition has been described. I should not subscribe to that diagnosis. I am more inclined to look for the individual papules of lichen planus, but the histologic section certainly shows the considerable sclerosis with areas of lymphocytic infiltration which one sees at the base of the lesions of sclerosing lichen planus.

Lymphogranulomatosis (Hodgkin's Disease): Treatment with Sulfanilamide. Presented by DR ERICH URBACH (by invitation)

S S, an undernourished white man aged 52, presents a widespread eruption exempting only the palms and soles. It consists of thickening of the skin, which is excoriated in places or covered with branlike brownish violet scales. The face shows distinct papules and crusted lesions. There is visible enlargement of the lymph nodes of the neck, axillas and groin, the nodes are hard and not coalescent.

The condition began in January 1938, as pruritic small erythematous patches on the arms. In rapid succession similar lesions appeared on different parts of the body, until by the end of four months the entire body was involved. There was almost unbearable pruritus. Five months after the onset, generalized adenopathy was noted. There was a loss of 12 pounds (5.4 Kg) in weight in the first six weeks of the disease. The patient was hospitalized in June 1938 at one hospital and in September and December at another. At this time a blood count showed 20,000 leukocytes per cubic millimeter, with 29 per cent eosinophils. A roentgenogram of the chest showed no evidence of glandular involvement. In September the spleen was found to be enlarged. A blood count showed 4,800,000 erythrocytes and 20,000 leukocytes per cubic millimeter, with 90 per cent neutrophils, 8 per cent lymphocytes and 2 per cent eosinophils. The sedimentation rate of the blood was 110 mm. The value for blood sugar was 85 mg per hundred cubic centimeters. Serologic tests of the blood gave negative results. In sections there were acanthosis and edema of the epidermis. In the stratum papillare and reticulare there was perivascular infiltration of small and large lymphocytes, epithelioid cells, plasma cells and a few eosinophilic cells. The blood and lymph vessels were enlarged. The section of lymph node showed decided hyperplasia of the reticular cells. Here and there cells suggesting Dorothy Reed giant cells were present. There has been remarkable improvement under treatment with sulfanilamide (36 Gm in nineteen days). The acute cutaneous lesions and the pruritus have almost disappeared, there has been a diminution in the size of the lymph nodes. The following data show the influence of treatment on the blood picture and on the sedimentation rate.

| | 1939 | | | |
|--------------------|--------|--------|--------|-------|
| | 4/28 | 5/5 | 5/8 | 5/15 |
| White cells | 20,000 | 12,300 | 10,400 | 8,100 |
| Neutrophils | 90 | 79 | 65 | 63 |
| Lymphocytes | 8 | 21 | 21 | 26 |
| Eosinophils | 2 | 6 | 14 | 11 |
| Sedimentation rate | 110 | 100 | 125 | 65 |

DISCUSSION

DR DONALD M. PILLSBURY: Although there were no cultural studies indicating the presence of streptococci, I think the number of cases in which such a condition responds to sulfanilamide is remarkable. Another case of generalized exfoliative dermatitis in a woman was presented tonight, in which the only reason for giving sulfanilamide was the fact that there were streptococci in the urine. I do not know why the present patient responded. Is there possibly some nonspecific effect of the drug? I think there is danger of becoming overenthusiastic about the use of sulfanilamide in such cases. I know that I have given the drug in my office on some occasions when, as I look back, I think I should not repeat the performance. I think one ought to be cautious about indiscriminate administration of sulfanilamide.

DR ERICH URBACH (by invitation): This man was so distressed that it was necessary to take him to the hospital. He had been previously hospitalized and had received much roentgen therapy as well as other forms of nonspecific treatment. The English school believes that Hodgkin's disease is a virus disease. I used sulfanilamide on this basis. It was interesting to see the progress in this case. I gave the first course of treatment cautiously for five days, 4 Gm daily, divided into ten doses. The treatment was then stopped, and the itching became less. The cutaneous lesions were also improved, so I waited. After four days there was a recurrence of the itching, and new lesions and fever developed. A second course was given, lasting three days. There was improvement again. I then gave 2 Gm in two days. I cannot say whether there will be a second relapse.

Lupus Erythematosus (Extensive Discoid) Presented by DR WILLIAM E KELLEY, Omaha (by invitation)

J M, a white man aged 44, shows diffuse erythema of the face, cheeks and ears. The lesions are slightly scaly, with hyperpigmented borders. The ears are red and tender, showing some atrophy of the rim. There are a few round areas of tender, red, slightly scaly patches on the back of the neck. The backs of the wrists and the forearms show bright red, slightly scaly, elevated gyrate lesions with atrophic centers. The arms and the V of the neck, the sites of previous involvement, show extensive areas of leukoderma. The edges of the lesions on the fingers are hyperpigmented. The patient was well until July 1936, when he went to the seashore for a week and received an extensive sunburn. This healed, but three weeks later little "pimples" began to break out on his face. In a few weeks the entire face, the "V" of the neck and the arms were involved. The following winter the condition cleared up completely, leaving the areas of leukoderma now seen. In the summer of 1937 it again flared up after an exposure to the sun, not so severe as the first. It cleared up again the following winter except for a small area on the left cheek. In the summer of 1938 the patient was on a farm for three days. A week later the lesions again flared up, this time with involvement of the upper lip and the backs of the wrists. Last winter it failed to clear up completely. The redness on the face and wrists persisted. A blood count showed 4,950,000 erythrocytes and 7,700 leukocytes per cubic millimeter. The value for hemoglobin was 87 per cent. A differential count showed 81 per cent polymorphonuclears, 12 per cent lymphocytes, 5 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils. The Wassermann, Eagle and Kahn reactions of the blood were negative. A roentgenogram of the chest showed the bony portion of the thorax, the heart and the aorta to be normal. There were scattered diffuse, small nodular areas of fibrosis throughout both lung fields, more marked in the upper outer third. As there was a clinical history of working ten years in a sand blast, this was undoubtedly due to silicosis. There was no evidence of tuberculosis or other secondary infection. In August 1936 the patient received fifteen injections of gold sodium thiosulfate, without improvement. At present he is receiving a bismuth compound.

DISCUSSION

DR ROBERT L. GILMAN: Some one commented that at first glance he thought the patient might have pellagra. Just what role dietary deficiency may play in this case and whether it may suggest additional therapeutic measures cannot be stated. The patient has been seen before, in other clinics. There was also some inquiry about the status of the leukoderma around the borders of the lesions on the neck. Since there are healing lesions and developing leukoderma about the elbows and the arms, it is reasonable to believe that the other depigmentation on the body is a direct result of the disease.

DR DONALD M. PILLSBURY: I think there is no question about the diagnosis on the appearance of the lesions, but I agree with Dr. Gilman that the emaciation and evidence of poor nutrition which this man presents are significant. I think this is a case of lupus erythematosus in which if one does not pay attention to the background one will not get anywhere. I suggest a high vitamin diet. Certainly treatment with gold compounds alone will not produce satisfactory results.

DR ERICH URBACH (by invitation): I should say that this condition is a subacute exacerbation of discoid lupus erythematosus, and I suggest a porphyrin study, since the man became affected after exposure to the sun. It has been shown that in some such cases porphyrin can be found only in the stool, and by changing the diet I have obtained some good results. I do not say that sensitiveness to light is the cause of lupus erythematosus, but it is one of the factors to be considered.

Rosacea with Keratitis and Corneal Ulceration Presented by Dr H P PARISER (by invitation)

B J, a white woman aged 51, well developed and not acutely ill, presents an erythematous eruption on the cheeks and about the eyes, associated with erythematous papules, particularly on the nose and chin. There is diffuse scaling of the scalp. The eyelids are reddened and the conjunctivas slightly injected. The left eye shows two minute corneal opacities and the right eye one. A small quantity of pus was expressed from the tonsillar crypts.

The patient had otitis media in 1936. She had aphonia in October 1937, which was cleared by inhalation and sprays. She has had constipation for many years. In November 1937 she had a profuse erythematous papular eruption on both cheeks, the nose and the chin and about the eyes. The eruption has improved partially at times but has flared repeatedly without apparent cause. In December 1938 the left eye became reddened and extremely painful, and there was severe photophobia. Local palliative treatment, roentgen therapy and injections of a gold compound at another institution were without appreciable effect on the skin or on the eye. Early in May 1939 the right eye became somewhat reddened and painful. Blood counts and urinalyses gave normal results, and serologic tests of the blood for syphilis, negative results. Analysis of the gastric contents showed no free hydrochloric acid before or after stimulation with histamine and a considerably diminished total acid content. A culture of material from the corneal lesion showed *Staphylococcus albus*. Roentgenograms of the chest showed probable old tuberculosis of the upper lobe of the right lung. Roentgenograms of the sinuses showed thickened mucous membrane in the ethmoid and maxillary sinuses. The results of tuberculin tests with old tuberculin, 0.1 cc of a 1:10,000,000 dilution and a 1:1,000,000 dilution, were negative, but the reaction to 0.00001 mg of purified protein derivative was positive. The eye was treated with atropine sulfate 1 per cent, 1 drop three times a day, and warm boric acid compresses for twenty minutes four times a day. An oxycholesterol-petrolatum ointment was prescribed for the skin. Internally the patient was given 1 drachm (3.69 cc) of dilute hydrochloric acid before meals and 1 drachm every hour for three hours after meals, also 2 drachms (7.38 cc) of calcium gluconate three times a day. Whole milk was given intramuscularly (flare-up?). Liquid petrolatum, sedatives and a soft diet were also prescribed. A tonsillectomy was performed on May 5, with slight improvement of the skin and less injection of the conjunctivas.

DISCUSSION

DR CARROLL S WRIGHT: Such cases are interesting from the standpoint of treatment. Two cases stand out particularly in my mind. One patient was sent to me some years ago by an ophthalmologist with the request that if I used roentgen rays I should expose the eye. There was remarkable improvement in the skin, and considerable improvement was noticed in the eyes. Recently I treated a girl aged 14 with this condition, I used extremely small doses of roentgen rays (not over $\frac{1}{8}$ skin unit) and did not cover the eyes with lead, the ocular condition became quiescent, and the rosacea disappeared. Of course, I placed the patient on a suitable diet, and Kummerfeld's solution was used locally. (The formula for Kummerfeld's solution is as follows: precipitated sulfur, 3.88 Gm, pulverized camphor, 0.32 Gm, pulverized tragacanth, 0.65 Gm, rose water, 30 cc, and solution of calcium hydroxide, 30 cc.) I think roentgen therapy is indicated for rosacea, together with other therapy.

DR DONALD M PILLSBURY: I do not believe that the diagnosis of rosacea has been definitely established. The lesions are definitely papular, which I think suggests the possibility of some tuberculous process. I have treated rosacea in a number of patients with keratitis by exposure of the eyes to roentgen rays. I do not think one takes a great risk. It should be considered that rosacea is often severe, and it is worth taking the slight risk of cataract formation to secure a good result. In a series of cases reported by Dr Cole of epithelioma in the

ocular region in which the eyes could not be completely protected, there was no instance of cataract in a long series of patients receiving heavy doses of roentgen rays. One should be cautious in most cases, but in this instance the risk is worth taking because it is not great.

DR JOHN H. STOKES: There is no necessary relation between severe or mild rosacea and so-called rosacea keratitis. Keratitis of identical type occurs in patients in whom one can identify the presence of the flush only in conversation. When the patient first comes into the office the rosacea cannot be seen, but after a few moments' talk the characteristic facial flush appears, this fades out after a short time. It does not necessarily follow that treatment of the rosacea will improve the keratitis or vice versa. I have treated a few patients with roentgen rays and have invariably exposed the eyes. The late Dr. Baer, an ophthalmologist, at first disapproved but subsequently approved my doing so in some of the cases we observed together, so I think it proper to expose the eyes. This type of case is also a good field for testing the nonspecific effect of gold sodium thiosulfate. Some of the patients show extreme sensitiveness to tuberculin, whatever that may mean, but when one uses 2, 3 or 5 mg. doses of gold sodium thiosulfate, one may occasionally, I think, see definite although temporary improvement.

DR ERICH URBACH (by invitation): At the clinic for diseases of the eye in Vienna, Austria, Dr. Kovacs Muller has used grenz rays extensively, with good results, in cases of this kind of keratitis.

DR THOMAS BUTTERWORTH, Reading, Pa.: In many pathologic conditions of the ocular regions objections to roentgen irradiation may be overcome by the use of the bare radium plaque. The penetration is much less and in many cases of stubborn lesions on the lids the results are good. For longer exposures I protect the eyeball with a 1 mm. chromium-plated brass shield after anesthetizing the conjunctival sac with 2 per cent solution of phenacaine hydrochloride.

DR. ELMER R. GROSS, Wilmington, Del.: I suggest that milk be given a further trial. Good results in such cases have been obtained at the Wills Hospital (for the eye). The ophthalmologists at that hospital also are using grenz rays.

DR DONALD M. PILLSBURY: A grenz ray apparatus was secured for the University Hospital, which later gave up its use. There have been many favorable reports in Europe, the use of these rays around the eyes is safe because the penetration is very slight.

Generalized Lupus Erythematosus? Vitamin Deficiency (Pseudopellagra)? Dermatomyositis? Addison's Disease? Presented by DR. A. R. KAUFMAN, Wilkes-Barre, Pa.

A. K., a white man aged 29, presents mahogany pigmentation of the face with moderate cyanosis of the chin. The ears show some evidence of powder lesions from the mines. On the dorsum of each hand, especially around the proximal phalanges, there is pigmentation with atrophy. The right elbow is brawny to the touch and tender. For about one week, in March 1939, the patient noticed swelling of the face for about one day. After this he noticed pigmentation of the face and applied for treatment. Since then the pigmentation has become progressively deeper and the right elbow has started to swell. He has also had weakness and vague pains in various joints.

DISCUSSION

DR ERICH URBACH (by invitation): The condition looks like pseudopellagra of alcoholic origin. This man eats little, but he has a tendency to drink to excess.

DR JOHN H. STOKES: I have seen examples of disseminate erythematous lupus in which sudden infiltrations of muscle tissue occurred. They sometimes resolved and sometimes broke down with a discharge of pus. I remember one young man particularly who presented a frightful example of the latter occurrence. He lost a large part of the calf of his leg in one such infiltration followed by

breakdown in the course of disseminate erythematous lupus I do not know just how one could bring the possible myositis into the diagnosis of alcoholic pseudo-pellagra I questioned the patient about trauma, and he said he could not remember any injury Of course, when I first looked at the man I hoped I was seeing flexure of the biceps due to syphilis, which seems to have occurred in France and nowhere else

DR A R KAUFMAN, Wilkes-Barre, Pa Talbott, Gall, Consolazio and Coombs (*Arch Int Med* 63 476-496 [March] 1939) described dermatomyositis with scleroderma and calcinosis, and the early picture in the case those authors described seems to agree with that in this case That is the reason I included that condition among the possible diagnoses

Exfoliative Dermatitis Treated with Sulfanilamide Presented by DR JAMES MURLIN FLOOD (by invitation)

E P, a white woman aged 60, in fair condition, presents universal erythematous and weeping exfoliative dermatitis An appendectomy and a cholecystectomy were performed in the summer of 1938 In 1936, three days after receiving a permanent wave (heat method) she noticed unusual scaling of the scalp This progressed, and the hair began to come out in "handfuls" The scaling continued, involving the ears and neck and gradually the whole body The last portion of the body to become involved was the face There have been periodic regressions and exacerbations with no apparent definite cause The present episode started at the end of March 1939 and has become progressively worse The itching has become intolerable, by April 20 the patient was hysterical and was receiving large doses of sedatives One blood count revealed 4,180,000 erythrocytes and 5,200 leukocytes per cubic millimeter, 78 per cent hemoglobin, 53 per cent polymorphonuclear leukocytes, 30 per cent lymphocytes, 11 per cent monocytes and 6 per cent eosinophils A blood count after the administration of sulfanilamide showed 2,500,000 erythrocytes and 11,000 leukocytes per cubic millimeter, 48 per cent hemoglobin, 76 per cent polymorphonuclear leukocytes, 19 per cent lymphocytes, 2 per cent monocytes, and 3 per cent eosinophils Urinalysis showed a few granular and hyaline casts but no arsenic Cultures of the urine showed a moderate number of hemolytic staphylococci (*Staphylococcus aureus*), an occasional colon bacillus, some specimens of *Bacillus subtilis* and nonhemolytic streptococci The Kolmer and Kahn reactions of the blood were negative A roentgenogram of the chest was normal Histologic examination of the skin showed exfoliative dermatitis Study of the bone marrow showed it to be normal The patient was given sulfanilamide as follows 90 grains (5.7 Gm) per day for five days, 80 grains (5.17 Gm) per day for six days, 50 grains (3.24 Gm) for one day, 30 grains (1.94 Gm) for one day It was stopped because of the falling erythrocyte count Cholesterolized petrolatum and dusting powder were applied locally At the time of admission paraldehyde and chloral hydrate were given for sedation

DISCUSSION

DR E R GROSS, Wilmington, Del This patient states that she has lived on a farm all her life and has occasionally helped in the fruit picking The fruit may have been sprayed with arsenate of lead

DR DONALD M PILLSBURY There is no arsenic in the urine The hair and nails were not studied In spite of the severe dermatosis, one cannot demonstrate anything abnormal on examination except the changes in the skin, the urinary infection and the history of a severe nervous upset a few years ago I do not know whether the nervous upset has any connection with the dermatitis

A Case for Diagnosis (Pustular Psoriasis? "Id"?) Presented by DR DONALD M PILLSBURY

R A D, a white man aged 44, well developed and apparently healthy, presents subsiding scaling erythematous papules on both elbows There is a superficial

erythematous patch on the right knee and the right pretibial surface. Both hands and feet present sharply outlined patches of small pustules, which are inflammatory at their onset. The pustules show no tendency to extend peripherally. The finger nails are raised at the free border and show some discoloration (probably due to applied medication) and pitting. Near the base they are fairly normal in appearance. General physical examination gave essentially negative results. There are no demonstrable foci of infection. Eleven months ago the patient had a papulo-squamous eruption of the elbows, pretibial surface and scalp and recurrent vesiculopustular lesions in sharply margined patches on the hands and feet. All the finger nails and toe nails have been involved. Scrapings from the lesions (one examination) did not reveal fungi. The intradermal trichophyton test and the staphylococcus ambotoxoid test gave negative results.

DISCUSSION

DR CARROLL S WRIGHT. In some 40 cases of psoriasis in which I have tried extensive use of vitamin D, I included a patient similar to this, who was the only one in whose case I felt that I obtained a striking result. This patient had been seen by other dermatologists in different cities and had been treated with sodium cacodylate with temporary improvement, but she continued to relapse. I gave her 300,000 units of vitamin D during about four months. At the end of that time the lesions disappeared, and after eight months she has had no recurrence. One case does not make a series, of course. When I started the vitamin D treatment no other therapy was used.

DR DONALD M PILLSBURY. I do not know whether the patient has pustular psoriasis or not, but the picture is suggestive. I have treated 2 patients with this type of eruption with sulfanilamide. One became well, the other did not improve. I feel that in some of these cases staphylococcus ambotoxoid has at times been definitely helpful. If the patient has a positive reaction I give a 1 to 10 dilution of ambotoxoid intracutaneously.

DR JOHN H STOKES. Speaking of the ambotoxoid, I think a good many of these patients either have hemolytic staphylococcus infections at the start or acquire them as complications of the process and that they are the part of the condition that responds to the toxoid. The way in which I deal with them is not curative, and I have nothing so definite to offer as Dr Wright's use of vitamin D, but I think that if the patient can be induced to do the necessary amount of work for about two years, he can gradually bring the infection, if it is such, and its sensitization background under control. In cases in which the process occurred on the heels I have found certain shoe insoles to be contributing factors. When it occurs on the palms one cannot find so satisfactory a cause. I paint the lesions with Castellani's carbolfuchsin paint over and over again. I use sandpaper day after day, when the vesicular phase disappears or is reduced to a minimum, I paint the lesions with a crude coal tar-acetone-collodion paint. If there are any recognizable allergic elements, they should be dealt with, by diet or otherwise, and the nervous state of the patient should have some attention. I have seen hands and feet similarly affected improve for considerable periods after vacations. I remember a young man in whom the condition cleared up and remained well for a long period after a two week trip through the South with the driver of an oil tank. He sat beside him on the box and did nothing but put his feet against the motor, which was as hot as one can imagine. His hands and feet recovered. I have seen patients recover on automobile trips in which they rode with the driver, and I have seen them get worse driving their own cars. I think the persistent mechanical and antiseptic attack on these lesions together with recognition of the fact that they are probably associated with a virus or a hemolytic staphylococcus infection or both, and the attempt to deal with the staphylococcal infection if possible are about as good treatment as I know of at present. I dare say none of the members now is abusing these patients with roentgen rays. Some of them not only do not become better under roentgen ray treatment but become definitely worse.

Book Reviews

The Merck Index Fifth Edition Price, \$3 Pp 1060 Rahway, N J
Merck & Co, Inc, 1940

The Merck Index, the first edition of which appeared in 1889, now covers more than 1,000 pages, twice the number of the previous edition, which was published in 1930. It is definitely swelling by accretion. It offers as one of its new features "Chemical, Clinico-Chemical Reactions, Tests and Reagents by the Author's Name" (350 pages). Many of these references have only historical value. However, the volume contains much valuable information.

News and Comment

EXAMINATION BY AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

The next examination will be given by the American Board of Dermatology and Syphilology at the time of the annual meeting of the American Academy of Dermatology and Syphilology in November 1940 unless sufficient applications have been filed with the secretary before March 1 to make it worth while to hold an examination in New York at the time of the meeting of the American Medical Association, June 10 to 14, 1940.

DEATH OF DR CHARLES AUGUSTUS SIMPSON

Dr Charles Augustus Simpson, of Washington, D C, died suddenly on Dec 9, 1939.

Directory of Dermatologic Societies *

INTERNATIONAL

TENTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY

Oliver S Ormsby, President, 25 E Washington St, Chicago
Paul A O'Leary, Secretary-General, 102-2d Ave S W, Rochester, Minn
Place New York Time Summer 1940

PAN AMERICAN MEDICAL ASSOCIATION, SECTION OF DERMATOLOGY AND SYPHILOLOGY

Elmore B Tauber, President, 19 W 7th St, Cincinnati
Austin W Cheever, Secretary, 49 Bay State Rd, Boston

FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY (CANADIAN BRANCH)

L P Ereaux, President, 1390 Sherbrooke St W, Montreal
F E Corma, Secretary-Treasurer, 2068 Sherbrooke St W, Montreal

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY

H W Barber, President, 7 Devonshire Pl, London, W 1, England
Louis Forman, Secretary, 7 Devonshire Pl, London, W 1, England

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

John G Downing, Chairman, 520 Commonwealth Ave, Boston
C F Lehmann, Secretary, 705 E Houston St, San Antonio, Texas
Place New York Time June 10-14, 1940

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY

Paul A O'Leary, President, Mayo Clinic, Rochester, Minn
Earl D Osborne, Secretary, 471 Delaware Ave, Buffalo, N Y
Place Philadelphia

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

Howard Fox, President, 140 E 54th St, New York
C Guy Lane, Secretary-Treasurer, 416 Marlborough St, Boston

AMERICAN DERMATOLOGICAL ASSOCIATION

Frank C Knowles, President, 2035 Spruce St, Philadelphia
Fred D Weidman, Secretary, University of Pennsylvania, Philadelphia

SOCIETY FOR INVESTIGATIVE DERMATOLOGY

Joseph V Klauder, President, 1934 Spruce St, Philadelphia
S W Becker, Secretary, University of Chicago, Department of Medicine, Chicago

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date

SECTIONAL

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

John C Kerr, President, 621-14th St, Wheeling, W Va
 Marvin B Goldstein, Secretary-Treasurer, Stambaugh Bldg, Youngstown, Ohio
 Place Buffalo, N Y Time Spring 1940

MISSISSIPPI VALLEY DERMATOLOGICAL SOCIETY

Hamilton Montgomery, President, Mayo Clinic, Rochester, Minn
 Herbert Rattner, Secretary-Treasurer, 25 E Washington St, Chicago
 Place Chicago

NEW ENGLAND DERMATOLOGICAL SOCIETY

J Harper Blaisdell, President, 83 Marlborough St, Boston
 Bernard Appel, Secretary, 483 Beacon St, Boston

NORTHERN NEW JERSEY DERMATOLOGICAL SOCIETY

Louis J B Le Bel, President, 165 Grant Ave, Nutley
 C C Carpenter, Secretary, 38 Waldron Ave, Summit
 Place Academy of Medicine of Northern New Jersey, Newark Time Third
 Tuesday of March, April, October and December

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CUTANEOUS CARBOHYDRATES

I THE NORMAL SKIN

THEODORE CORNBLEET, M D

CHICAGO

The metabolism of carbohydrates in normal and in pathologic skin has been studied by a number of investigators without revealing its general pattern. A few isolated facts related to this problem have been ascertained, but relatively few of definite and unquestioned significance. There is disagreement about even some of the fundamentals. The solution of the problem has been difficult in many respects because of the lack of reliable quantitative methods of analysis for small portions of skin. Relatively recent developments have improved this situation. Consequently it seems propitious to again make a careful analysis and survey of the dextrose and glycogen content of normal skin, so that comparisons with pathologic skin may be more significant.

A rather wide range of values has been quoted for the normal dextrose content of human skin. Only those of rather recent publication are considered here, since the older methods of determining such values are not considered reliable. Urbach and Sicher¹ in 1929 and Urbach and Rejto² in 1932 found the normal value for dextrose to be 47 mg per hundred grams of skin, and in 1937 with a refined method, Urbach, Depisch and Sicher³ reported 61 mg. Trimble and Carey⁴ in 1932

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1 Urbach, E, and Sicher, G. Beiträge zu einer physiologischen und pathologischen Chemie der Haut. III. Der Zuckergehalt der Haut unter physiologischen und pathologischen Bedingungen, *Arch f Dermat u Syph* **157**:160, 1929

2 Urbach, E, and Rejto, K. Beiträge zu einer physiologischen und pathologischen Chemie der Haut. XI. Ueber den freien und "gebundenen" Zucker in der Haut unter physiologischen, experimentell veränderten und pathologischen Bedingungen bei Mensch und Tier, ein Beitrag zum Kohlehydratstoffwechsel der Haut, *Arch f Dermat u Syph* **166**:478, 1932

3 Urbach, E, Depisch, F, and Sicher, G. Zum Problem des isolierten hohen Hautzuckers bzw Hautdiabetes, *Klin Wchnschr* **16**:452, 1937

4 Trimble, H, and Carey, B W, Jr. On the True Sugar Content of Skin and of Muscle in Diabetic and Non-Diabetic Persons, *J Biol Chem* **90**:655, 1931

studied what they called the true sugar value of normal human skin, finding 56 mg. The figures for animal skin vary considerably with different species but are fairly constant for any particular species. For dogs various authors⁷ report from 60 to 101 mg, for rabbits from 105 to 155 mg, for mice from 53 to 81 mg and for rats from 80 to 104 mg.

Few reliable reports on the glycogen content of human or animal skin are to be found in the literature. Fahrig⁶ found about 71 mg per hundred grams of what he calls the inner true skin and 157 mg for the same amount of outer skin of human beings. Pillsbury and Sternberg⁷ determined the glycogen content of the skin and liver of dogs on various diets and found in the skin about 108 mg with a low carbohydrate diet, 137 mg with a high carbohydrate diet and 75 mg with a high fat, low carbohydrate diet. Variations in the liver were much greater than those in the skin. Narahara^{5b} found glycogen in the skin of rabbits ranging from 5 to 67 mg, with an average of 34 mg. Gualdi and Baldino⁸ and Yuyama⁹ microscopically detected in the sweat glands considerable glycogen, eliminated largely during functional activity. Matsumoto^{5c} found in normal rabbit skin a glycogen content of 86 mg. The figures for glycogen are variable and indicate that the methods may be not entirely satisfactory or at least not standardized.

The areas from which the samples of skin are taken must be considered. Fahrig⁶ found 0.2269 mg of glycogen per hundred grams of human epidermis from the mammary region, and 0.3442 mg in that from the leg. Matsumoto^{5c} found that the sugar content of the skin

5 (a) Pillsbury, D. M., and Kulchar, G. V. The Use of the Hagedorn-Jensen Method in the Determination of Skin Glucose, *J. Biol. Chem.* **106** 351, 1934. Urbach and Sicher¹. Trimble and Carey¹. (b) Narahara, K. Experimentelle Untersuchung über den Hautzucker. IX. Hautglykogen und Zuckerabbau in der Haut, *Jap. J. Dermat. & Urol. (Abstr. Sect.)* **35** 31, 1934, abstracted, *Biol. Abstr.* **9** 1727, 1935. (c) Matsumoto, Y. An Experimental Study of the Carbohydrates of the Skin, with Special Reference to the Combined Sugar (Protein Sugar) and the Glycogen. I, *Mitt. a. d. med. Akad. zu Kyoto* **7** 1307, 1933. (d) Matsumoto, Y. II, *ibid.* **8** 481, 1933. (e) Moncorps, C., Bohnstedt, R. M. and Schmid, R. Ueber den Zucker- und Glutathiongehalt von Blut und Haut bei Hahnen- und Crotonoldermatitis, ein Beitrag zur Frage peripherisch bedingter Stoffwechselvorgänge, *Arch. f. Dermat. u. Syph.* **169** 67, 1934.

6 Fahrig, C. Ueber den Kohlehydratumsatz der Geschwulste und ihrer normalen Vergleichsgewebe sowie seine Beziehungen zum Milchsäurehaushalt des Körpers, *Ztschr. f. Krebsforsch.* **25** 146, 1927.

7 Pillsbury, D. M., and Sternberg, T. H. Relation of Diet to Cutaneous Infection, *Arch. Dermat. & Syph.* **35** 893 (May) 1937.

8 Gualdi, A., and Baldino, N. Ricerche sul metabolismo per variazioni della temperatura locale dei tessuti, il contenuto in glicogeno e in acido lattico della cute e dei muscoli raffreddati, *Riv. di pat. spec.* **5** 318, 1930.

9 Yuyama, H. Ueber die histologische Untersuchung der Glykogenverteilung in der leprosen Haut, mit besonderer Berücksichtigung der Beziehung zwischen der Funktion der Schweißdrüsen und der Schwankung des Glykogens. *Jap. J. Dermat. & Urol. (Abstr. Sect.)* **37** 134, 1935.

of the back was lower than that of other parts, while the glycogen content was highest in the skin of the back, less in that of the flank and least in that of the abdomen and extremities Fahrīg found decided differences in the glycogen content of the outer and inner parts of the skin, as mentioned in the foregoing paragraph On account of these wide variations in observations among different authors one concludes

TABLE 1—*Summary of Prior Reports on Dextrose Content of Skin*

| Date | Authors | Dextrose, Mg /100 Gm | | | |
|------|--------------------------------|----------------------|--------------|--------|-------|
| | | Man | Dog | Rabbit | Mouse |
| 1927 | Folin, Trimble and Newman | | 67 (fasting) | | |
| 1929 | Urbach and Sicher | 47 | 60 | 117 | 53 |
| 1931 | Trimble and Carey | 56 | | | |
| 1932 | Urbach and Rejto | 47 | 84 | 134 | 53 |
| 1933 | Matsumoto | | | 112 | |
| 1933 | Matsumoto | | 91 | 114 | |
| 1934 | Narahara | | | 115 | |
| 1934 | Pillsbury and Kulchar | | | 105 | |
| 1934 | Moncorps, Bohnstedt and Schmid | | | | 81 3 |
| 1937 | Urbach, Depisch and Sicher | 61 | 101 | 155 | 69 |

TABLE 2—*Summary of Prior Reports on Glycogen Content of Skin*

| Date | Authors | Glycogen, Mg /100 Gm | | |
|------|--|---|--|----------------------|
| | | Man | Dog | Rabbit |
| 1903 | Schondorff, quoted by Rothman | 724 (Av)
(92 7 to 1,680) | | |
| 1927 | Fahrīg | 157 (outer true skin)
71 (inner true skin) | | |
| 1927 | Folin, Trimble and Newman, quoted by Rothman | | 17 (fasting) | |
| 1930 | Gualdi and Baldine | | 70 | |
| 1933 | Matsumoto | | 183 (tail) | 86
82 (G) |
| 1933 | Matsumoto | | | 87 (16) |
| 1934 | Narahara | | | 34 (Av)
(5 to 67) |
| 1937 | Pillsbury and Sternberg | | 108 (low carbohy
drate diet)
137 (high carbohy
drate diet)
75 (high protein
diet) | |
| | Tabulae biologicae, vol 3 | 61 | 26 (fasting) | |

that the method of taking samples, the areas from which samples are taken, the preparation of the skin for analysis and the methods of determining dextrose and glycogen must be standardized before one may expect to have agreement in results However, most investigations are based on comparative changes so that variations among different authors may not be significant enough to warrant dispute, provided each investigator determines his control value carefully

The ratio of cutaneous sugar to blood sugar, according to Urbach, Depisch and Sicher³ varies with different species but is constant for

each particular species. They reported a ratio of 61:103 (skin sugar:blood sugar) for human beings, 69:108 for mice, 101:96 for dogs, 104:83 for rats, 147:111 for guinea pigs and 155:108 for rabbits. Narahara^{5b} reported a ratio of 115:104 for rabbits. Matsumoto^{5c} reported 112 mg of sugar per hundred grams of normal rabbit skin. Sellen and Spiera¹⁰ observed a ratio of 139:108 in fasting rats and 180:174 when the rats were on a mixed diet. They used figures for total reducing substances, which they found to be 20 to 30 per cent higher than the actual sugar values. This again shows the necessity for standardization of procedures.

Various authors have investigated what has been called bound sugar, those reducing substances which remain in the protein precipitate, perhaps glycoproteins, and are released on acid hydrolysis. Urbach and Rejto² observed a greater percentage of bound sugar in the skin than in the blood and attached importance to the retention of it in the skin longer than in the blood after the feeding of dextrose. There are many possible reducing substances in various tissues which this method might separate and which would have no bearing on the normal metabolism of carbohydrates. Matsumoto^{5c,d} has determined values for combined sugar (protein sugar) in an attempt to correlate it with the skin metabolism. Rabbits normally had 194 mg of protein sugar per hundred grams of skin. This increased considerably after injection of dextrose. Up to the present it would seem that the importance of these bound sugars has not had wide acceptance. Intermediary carbohydrate metabolism may involve the interaction of various combinations of reducing substances, but it seems evident from numerous investigations that dextrose and glycogen are the most important indicators of normal or disturbed carbohydrate metabolism.

No doubt diet plays a prominent role in determining the amount of sugar and glycogen in the skin. On carbohydrate-poor diets, according to Urbach and Sicher,¹ the cutaneous sugar was 12 per cent lower (61 mg) than on a carbohydrate-rich diet (73 mg), while the amount of sugar in the blood remained practically at the same level with both diets. As previously mentioned, Pillsbury and Sternberg⁷ found a higher glycogen content (157 mg) in dogs fed a high carbohydrate diet than in those with a high fat and low carbohydrate diet (75 mg). Rothman¹¹ stated that since with overfeeding the glycogen content of the cells of the skin, as well as that of the liver and muscle, was greater than that of the blood, it appeared that these cells built glycogen from lower carbohydrates. In all experimental work one can see the need of

10 Sellen, C., and Spiera, M. Die Rolle der Haut im Kohlenhydratstoffwechsel, *Biochem Ztschr* 296 83, 1938.

11 Rothman, S. Kohlenhydrate der Haut, in Jadassohn, J. Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol 1, pt 2, p 268.

carefully controlling the diet, especially when attempting to establish normal values for carbohydrates of the skin

With the administration of dextrose orally, the cutaneous sugar values parallel the blood sugar curve with a lag³. The cutaneous sugar reaches its peak in about one hour and returns to normal in about three hours, as compared with one-half and two hours, respectively, for the blood. The changes in cutaneous sugar thus appeared to be due to a simple diffusion process. In pathologic skin the normal diffusion processes might be disturbed, so that such a relation between blood and cutaneous sugars would not be entirely comparable. In patients with diabetes and in depancreatized dogs Urbach observed that the cutaneous sugar rose much more decidedly and was maintained for a much longer period than was the blood sugar. Narahara^{5b} found only slight variations in the cutaneous glycogen in the rabbit after feeding of dextrose, in spite of decided changes in cutaneous and blood sugar. Matsumoto^{3c} injected dextrose in the ear vein of the rabbit and found parallel changes in the sugar content of skin and blood over a period of two hours, while the glycogen content remained practically unchanged with doses up to 1 cc of a 40 per cent solution of dextrose. Two cubic centimeters of 40 per cent dextrose raised the cutaneous glycogen from 83 mg to 133 mg per hundred grams of skin in one hour (back to 74 mg in two hours), while the cutaneous sugar was raised from 123 mg to 251 mg. Ordinarily the increase in cutaneous glycogen may be a rather slow process, and considerable time may therefore be required to determine changes. Sellei and Spiera¹⁰ determined the total reduction power of the skin and blood in rats and found parallel curves after subcutaneous injection of dextrose, substantiating the belief in a simple diffusion process for the change in cutaneous sugar. Cori¹² found that 17 per cent of the orally given dextrose absorbed in rats was converted into hepatic glycogen in three to four hours. About 45 to 50 per cent was oxidized (metabolism experiments)¹³. About 36 per cent of the administered dextrose was found in the form of glycogen in the remainder of the body, which Cori assumed to be chiefly in the muscle. Determinations of cutaneous glycogen were not made, although a considerable part of the body glycogen might have been found there. The hepatic glycogen had reached its peak in about four hours and declined during the fifth hour in spite of continued absorption of sugar from the intestine. "Thus the par-

12 Cori, C. F. The Fate of Sugar in the Animal Body. III. The Rate of Glycogen Formation in the Liver of Normal and Insulinized Rats During the Absorption of Glucose, Fructose and Galactose, *J Biol Chem* **70**:577, 1926.

13 Cori, C. F., and Cori, G. T. The Fate of Sugar in the Animal Body. II. The Relation Between Sugar Oxidation and Glycogen Formation in Normal and Insulinized Rats During the Absorption of Glucose, *J Biol Chem* **70**:557, 1926.

icipation of the liver in the disposal of sugar is negligible in the later periods of absorption." The skin may then play a more prominent role in the formation of glycogen. Cori suggested, however, that the muscle was probably the most important organ in glycogen storage. Folin, Trimble and Newman¹⁴ gave dextrose intravenously to dogs and found the glycogen in the muscle only slightly higher thirty minutes after injection. From guinea pigs they were able to recover practically all the injected dextrose as free sugar in thirty minutes, analyzing the whole animal. There was, however, unequal uptake of sugar in various tissues analyzed individually. Practically no glycogen was stored during

TABLE 3—*Effect of Intravenous Injection of Dextrose on Glycogen Content of Skin of Dogs*

| Experiment | Glycogen, Mg /100 Gm | |
|------------|----------------------|--------------------------------|
| | Before Injection | Thirty Minutes After Injection |
| 1 | 1,085 | 1,147 |
| 2 | 1,042 | 1,108 |

TABLE 4—*Effect of Injection of Dextrose on Dextrose Contents of Blood, Skin and Muscle in Dogs*

| Experiment | Dextrose Thirty Minutes After Injection, Mg /100 Gm | | |
|--------------------------|---|------|--------|
| | Blood | Skin | Muscle |
| 1 | 412 | 390 | 154 |
| 2 | 360 | 276 | 89 |
| 3 | 286 | 322 | 141 |
| Average for fasting dogs | 84 | 67 | 54 |

that time. The cutaneous sugar closely followed the blood sugar, while the muscle sugar was much lower. They stated:

One important outlet for sugar as it leaves the blood is the skin. The skin, however, is not a storage place for glucose or glycogen, for in the fasting condition (? hours) it contains practically no glycogen and only a trifle more sugar than the muscle.

If the dogs fasted only twenty-four hours, it is difficult to understand the failure of Folin and his co-workers to find glycogen in the skin. It would be reasonable to expect that prolonged fasting would deplete supplies of glycogen in all parts of the body. This would not indicate a lack of ability on the part of the skin to store glycogen any more than it would on that of the liver. Determinations of glycogen several hours after the feeding of dextrose would be needed to refute

¹⁴ Folin, O., Trimble, H. C., and Newman, L. H. The Distribution and Recovery of Glucose Injected into Animals, *J Biol Chem* 75: 263, 1927.

or substantiate such an opinion Cori¹⁵ found that absorption of dextrose by the stomach takes place at a constant rate over several hours. Nevertheless, the blood sugar soon reaches its maximum in spite of the continued absorption, showing that the tissues after a short latent period take care of the dextrose as rapidly as it is absorbed from the intestine. Since tissue sugars also reach their peak in an hour or so, the further absorbed dextrose must be either burned or stored as glycogen. Folin and his associates¹⁴ state

As a temporary receptacle in response to sugar injections, the skin seems to us to be of much greater importance than heretofore appreciated. So far as concerns the influx of sugar into the skin, we have a number of experiments which seem to indicate clearly that the influx is the result of passive diffusion rather than of any special absorption or metabolic process.

Urbach, Depisch and Sicher,³ on the contrary, saw in the elaborate intermediate carbohydrate metabolism in the skin, as well as in the variations in the cutaneous sugar level and tolerance curve, sufficient reason to deny emphatically any mere diffusion phenomenon.

The intrinsic metabolism of carbohydrates in the skin is still poorly understood. Various factors have been investigated in an attempt to throw more light on this problem. Pillsbury¹⁶ studied the lactic acid content of rabbit skin and found about twice as much in the skin of well fed animals as in that of starved ones. In incubated skin he determined a normal curve for lactic acid production and found an increase when dextrose solution was added and still more when the solution was buffered with phosphate. Skin from rabbits given 3 Gm of dextrose intravenously one-half hour previously produced about twice as much lactic acid as did controls. There must therefore be enzymes present in the skin that make possible the transformation of dextrose with production of lactic acid. Fahrig⁶ presented evidence to support these findings. Moncoirps, Bohnstedt and Schmid^{5e} studied the sugar and glutathione contents of the skin of white mice and found that inflammation produced by irradiation caused changes in the amount of cutaneous sugar but practically none in that of glutathione. Nakamura¹⁷ investigated acetaldehyde formation in incubated skin. He found small amounts in fresh human and guinea pig skin, whereas cadaver skin (twenty-four hours) was entirely without it. The addi-

15 Cori, C. F. The Fate of Sugar in the Animal Body. I. The Rate of Absorption of Hexoses and Pentoses from the Intestinal Tract, *J. Biol. Chem.* **66**:691, 1925.

16 Pillsbury, D. M. The Intrinsic Carbohydrate Metabolism of the Skin. Preliminary Report of Experimental Studies, *J. A. M. A.* **96**:426 (Feb. 7) 1931.

17 Nakamura, Y. Die Fermente der Haut. IV. Ueber den Zuckerabbau in der Haut, *Biochem. Ztschr.* **173**:258, 1926.

tion of dextrose or glycogen increased the production of aldehyde in normal skin. Seller and Spiera¹⁰ blocked the reticulo-endothelial system of the rabbits with injections of water blue and a gold salt, aurolin, and found that while this caused the blood sugar to remain stationary or to decrease, the cutaneous sugar rose. They concluded that the reticuloendothelial system has some function in carbohydrate metabolism.

The question of the storage of carbohydrate in the skin is important, since the skin comprises about 16 per cent of the entire body tissues by weight or three times that of the liver. Urbach and Rejto² found that after dextrose was fed, the skin retained sugar much longer than did the blood, especially in depancreatized dogs, and concluded that the skin was an important temporary storage organ for sugar. Since high cutaneous sugar is possibly a factor in the severity of certain diseases of the skin, an antidiabetic regimen would be indicated in such conditions, especially if a dextrose tolerance test showed the cutaneous sugar to be abnormally high. Carrie and Koenig¹⁸ have shown that patients with high blood sugar excrete abnormally large amounts of sugar onto the skin surface and are more prone to cutaneous diseases, therefore requiring more frequent bathing as a prophylactic treatment. The presence of large amounts of sugar in the skin when blood sugar is high merely supports the theory that a simple diffusion process maintains cutaneous sugar levels and does not indicate storage. In rabbits Narahara^{5b} found that after ingestion or intravenous injection of dextrose the level of the cutaneous glycogen changed relatively little in spite of decided changes in the levels of blood sugar and cutaneous sugar. He therefore concluded that the skin was an important temporary receptacle for sugar but that it played little part as a storage organ for intermediary carbohydrate metabolism.

The importance of insulin in general body carbohydrate metabolism is well known and may be of considerable importance in the intrinsic carbohydrate metabolism and general health of the skin. Nakamura¹⁷ in his investigation of the acetaldehyde formation in the skin observed that when insulin was added to a mixture of skin and dextrose and incubated, there was an increased production of aldehyde with cadaver skin but little change with normal skin. The probable reason for this is that normal skin already has an optimal amount of insulin present to carry on normal metabolism, while insulin is lacking in the cadaver skin. Insulin normally present in the tissues thus appears to play a significant role in cutaneous carbohydrate metabolism. Urbach and Sicher¹ have noted that insulin in amounts sufficient to produce con-

18 Carrie, C., and Koenig, R. Ueber den Zuckergehalt auf der Haut bei Normalen und Diabetikern, *Arch f Dermat u Syph* **173** 611, 1936

vulsions in dogs caused a greater fall in blood sugar (90 mg to 43 mg per hundred cubic centimeters) than in cutaneous sugar (50 mg to 30 mg per hundred grams). In rabbits a blood sugar of 132 mg fell to 25 mg, while a cutaneous sugar of 142 mg fell to 53 mg. They pointed out a normal parallelism between blood and cutaneous sugar curves, but storage and retention of sugar in the skin took place in some cases. Leyton¹⁹ expressed the belief that local insulin packs are beneficial in some cases of obstinate septic lesions of the skin through a stimulation of local carbohydrate metabolism. Seller and Spiera¹⁰ found that after insulin was injected subcutaneously in rats there was a decrease in the cutaneous reducing substances from a normal of 139 mg to 120 mg with 4 units of insulin and an increase of reducing substances to 158 mg with 30 units. The blood reducing substances at the same time fell respectively to 45 mg and 55 mg from a normal level of 108 mg. They interpreted their results as indicating that after the injection of large amounts of insulin the skin endeavors for a certain time to act as a storage organ for carbohydrate. Corn and Corn¹⁸ found that rats receiving injections of insulin and being given dextrose by mouth absorbed the same amount of sugar as the controls without insulin but deposited less glycogen and oxidized more dextrose. They expressed the belief that since a large percentage of the carbohydrate metabolism took place in the muscle, a condition developed with excess insulin whereby the muscle utilized larger amounts of dextrose and therefore left less for the liver to convert into glycogen. If the figures of various authors are comparable, one finds that with insulin the sugar of the skin was reduced, but not as much as that of the blood.¹ The total reducing substance was lessened with small amounts of insulin and increased with large doses.¹⁰ This might indicate that up to an optimal amount insulin increases the metabolism of sugar in the skin but to a much less extent than that in the muscle. Therefore the cutaneous sugar is reduced and at the same time glycogen is deposited in the skin at an accelerated rate when there is excess of insulin. This tends to retain carbohydrate in the skin as a reserve supply.

Epinephrine is a normal circulating hormone which also has influence on carbohydrate metabolism, possibly of importance to the skin itself. Matsumoto^{5a} injected it into rabbits, with the results shown in table 5. After the administration of the drug the cutaneous sugar rose as a consequence of the rise in blood sugar, whereas the glycogen decreases. This indicates that epinephrine given systemically mobilizes sugar, derived in part perhaps from the cutaneous glycogen. It is

¹⁹ Leyton, N. Insulin in the Local Treatment of Persistent Septic Cutaneous Conditions, *Brit M J* 1:70, 1938

impossible to decide in this experiment whether the increase in cutaneous sugar is due only to simple diffusion from the blood or partly to conversion of some of the cutaneous glycogen present

The presence of many diverse local substances may influence cutaneous carbohydrate metabolism. Many physiologic experiments and clinical experiences have shown that histamine in the skin will dilate the capillaries and increase their permeability. It would therefore be logical to assume that abnormally large amounts of histamine produced locally or applied locally might affect the carbohydrate content of the skin by allowing more rapid diffusion of sugar from the blood stream into the skin than demanded by local metabolism, resulting in an abnormally high level of cutaneous sugar. On the contrary, epinephrine applied locally decreases the circulation of blood in the area. This may result in decreasing the diffusion of dextrose into the skin and thus lead to a disturbance in carbohydrate metabolism.

TABLE 5—*Effect of Injection of Epinephrine on Sugar and Glycogen Contents of Skin of Rabbits*

| | Sugar,
Mg /100 Gm | Glycogen,
Mg /100 Gm |
|-------------------------|----------------------|-------------------------|
| Before injection | 107 | 127 |
| 2 hours after injection | 221 | 108 |
| 5 hours after injection | 94 | 104 |

The application of heat locally is known to be beneficial in many cutaneous conditions, probably because it improves local circulation and aids the normal metabolism of the tissue. Ultraviolet irradiation and exposure to the sun's rays have been shown²⁰ to have a tendency to be followed, if mild, by a fall in blood sugar on the third or fourth day of from 22 to 25 mg per hundred cubic centimeters and, if productive of a rather severe erythema, by a rise of 18 to 25 mg. In white mice after ninety minutes' irradiation of the skin the cutaneous dextrose rose from a normal of 81 mg per hundred grams of skin to as high as 165 mg within eight hours. Cutaneous glutathione also rose from 76.1 mg to 155 mg. Inflammation induced by application of croton oil caused the dextrose tolerance curve of the skin to rise much higher than that of normal skin. The changes produced were possibly due to local variations in diffusion of histamine, epinephrine or dextrose. Meyer²⁰ showed that certain doses of ultraviolet radiation increased the ferment action in the skin of rabbits as judged by an increased production of purpurogallin. Doses up to 2 Finsen units increased the production from 0.16 to 0.172, 2.5 units decreased it to 0.135, and

20 Meyer, H. Alte und neue experimentelle Untersuchungen zur Wirkung des Lichtes, Strahlentherapie 23: 369, 1926

still higher doses brought ferment activity to an end. All ferments which have to do with carbohydrate metabolism in the skin are very likely influenced by ultraviolet rays.

The beneficial action of 1000 röntgen rays in clearing up some cutaneous lesions may also be partly due to changes in the metabolism of the cutaneous cells. David²¹ found that in general 1000 röntgen rays caused a dilatation of the cutaneous capillaries, probably through action on the Rouget cells. This may be the result of the formation of metabolites in the skin which in turn affect the Rouget cells. It is known that irradiation alters the oxidation and reduction reactions in tissues, and changes in the carbohydrate metabolism would therefore be expected.

With certain skin lesions the therapeutic use of various reducing substances leads to the recovery of normal tissue. Whether these effects are due to the action of such substances on abnormal factors present in the skin or to an improvement of the altered metabolism is not well known. However, since carbohydrate metabolism depends on various chemical transformations, reducing substances may have an important influence in this respect.

METHODS ADOPTED FOR DETERMINING THE AMOUNTS OF DEXTROSE AND GLYCOGEN IN THE SKIN

Dextrose—Samples of blood were drawn from fasting patients and at the same time portions of skin²² were taken from the back near the lumbar region. Ordinary biopsy punches, 9 mm in diameter, were used to remove a piece of skin weighing about 50 mg. This was finely minced and weighed and then transferred to a test tube containing 5 per cent zinc sulfate. The test tube was heated on a water bath for six minutes, and then 1 cc of tenth-normal sodium hydroxide and 0.5 Gm of a specially prepared fullers' earth (Lloyd's reagent) were added. The test tube was shaken for two minutes and the material filtered. The filter paper was washed three times successively with 2 cc of water. The dextrose in the filtrate was determined by the Hagedorn-Jensen method.

Glycogen—The skin sample removed weighed from 50 to 100 mg. This was placed in a 15 cc centrifuge tube to which was added 0.5 cc of a 30 per cent solution of potassium hydroxide. This was heated on a water bath until a clear solution was obtained, then 2 cc of 95 per cent alcohol was added, and the material was mixed and centrifuged. The supernatant fluid was discarded. The precipitate was washed twice with 2 cc of alcohol and was centrifuged after each washing. One cubic centimeter of 5 per cent sulfuric acid was added to the final washed precipitate. The material was heated on a water bath for one hour, cooled and neutralized with normal sodium hydroxide. The amount of dextrose in the neutralized solution was determined by the Hagedorn-Jensen method. From this the amount of glycogen was calculated.

21 David, O. Untersuchungen über den Einfluss von Röntgenstrahlen auf Kapillaren, Strahlentherapie 23:366, 1926.

22 Dr. H. C. Schorr helped to obtain biopsy material.

23 Footnote deleted.

TABLE 6—*Range of Values for Dextrose in Fifty-Six Subjects and Glycogen in Thirty-Three Subjects*

| Dextrose | | Glycogen |
|------------------|-------------------|------------------|
| Skin, Mg /100 Gm | Blood, Mg /100 Ce | Skin, Mg /100 Gm |
| 60.2 to 81.5* | 78.9 to 104.0* | 68.1 to 84.7 |

* Three subjects were found with higher values. One proved to be diabetic, and the others could not be followed. The results of the tests on these subjects are not included here.

TABLE 7—*Relation of Quantity of Cutaneous Dextrose and Glycogen to Layer of Skin* in Twenty Persons (Average Values)*

| | Superficial Skin,
Mg /100 Gm | Deep Layer,
Mg /100 Gm | Blood,
Mg /100 Ce |
|----------|---------------------------------|---------------------------|----------------------|
| Dextrose | 80.5 | 62.1 | 88.3 |
| Glycogen | 75.0 | 46.9 | |

* A biopsy specimen was taken down to the subcutaneous layer and then divided equally horizontally.

TABLE 8—*Dextrose Contents of Skin and Blood of Animals (Average Values)*

| Animal | Skin, Mg /100 Gm | Blood, Mg /100 Ce |
|------------|------------------|-------------------|
| Cat | 77.8 | 99.5 |
| Dog | 71.1 | 92.4 |
| Guinea pig | 104.7 | 148.2 |
| Rat | 77.2 | 127.6 |
| Rabbit | 96.9 | 160.3 |

TABLE 9—*Effect of Intravenous Injection of Dextrose on Content of Dextrose in Skin and Blood, and of Glycogen in Skin, of Six Dogs (Average Determinations)*

| | Dextrose | | Glycogen in
Skin,
Mg /100 Gm |
|--|----------------------|---------------------|------------------------------------|
| | Blood,
Mg /100 Ce | Skin,
Mg /100 Gm | |
| Control | 102.2 | 71.7 | 79.6 |
| After injection of dextrose, 4 Gm per kg | | | |
| ½ hour | 268.2 | 90.7 | 79.8 |
| 1 hour | 212.7 | 127.2 | 80.9 |
| 1½ hours | 180.7 | 155.8 | 81.7 |
| 2 hours | 120.2 | 102.7 | 83.6 |
| 2½ hours | 100.6 | 80.2 | 84.1 |

TABLE 10—*Effect of Injection of Insulin on Contents of Dextrose in Blood and Skin, and of Glycogen in Skin, of Five Dogs (Average Determinations)*

| | Dextrose | | Glycogen in
Skin,
Mg /100 Gm |
|---|----------------------|---------------------|------------------------------------|
| | Blood,
Mg /100 Ce | Skin,
Mg /100 Gm | |
| Control | 101.6 | 74.3 | 76.0 |
| After injection of insulin, 50 units intravenously and
50 units subcutaneously | | | |
| ½ hour | 87.6 | 66.8 | 76.6 |
| 1 hour | 61.1 | 60.4 | 82.1 |
| 1½ hours | 35.9 | 46.0 | 86.6 |
| 2 hours | 32.9 | 39.5 | 93.1 |

TABLE 11—*Effect of Subcutaneous Injection of Epinephrine on Content of Dextrose in Blood and Skin, and of Glycogen in Skin, of Five Dogs (Average Determinations)*

| | Dextrose | | Glycogen in Skin,
Mg /100 Gm |
|---|----------------------|---------------------|---------------------------------|
| | Blood,
Mg /100 Cc | Skin,
Mg /100 Gm | |
| Control | 88.3 | 66.4 | 75.6 |
| After injection of 0.05 cc of solution of epinephrine | | | |
| ½ hour | 99.7 | 80.1 | 77.6 |
| 1 hour | 113.8 | 93.0 | 81.2 |
| 1¼ hours | 124.3 | 104.8 | 82.9 |
| 2 hours | 145.6 | 120.9 | 86.9 |
| 3 hours | 163.7 | 150.2 | 93.8 |

TABLE 12—*Effect of Intracutaneous Injection of Epinephrine and Histamine on Content of Dextrose and Glycogen in Skin of Three Dogs (Average Determinations)*

| | Before Injection | | Ten Minutes After Intracutaneous Injection of Stated Solution | |
|------------------|-------------------------|-------------------------|---|-------------------------|
| | Dextrose,
Mg /100 Gm | Glycogen,
Mg /100 Gm | Dextrose,
Mg /100 Gm | Glycogen,
Mg /100 Gm |
| Area 1 (control) | 73.7 | 71.8 | (1 cc saline solution)
72.1 | 71.6 |
| Area 2 | 75.8 | 74.6 | (1 cc 1:5,000 epinephrine in saline solution)
60.7 | 72.1 |
| Area 3 | 76.7 | 75.2 | (1 cc 1:5,000 histamine hydrochloride in saline solution)
82.9 | 73.7 |

TABLE 13—*Influence of Elimination of Hepatic Circulation* on Content of Dextrose in Blood and Skin, and of Glycogen in Skin, of Three Dogs (Average Determinations)*

| | Dextrose | | Glycogen in Skin,
Mg /100 Gm |
|--|----------------------|---------------------|---------------------------------|
| | Blood,
Mg /100 Cc | Skin,
Mg /100 Gm | |
| Control | 106.2 | 71.8 | 77.6 |
| After elimination of hepatic circulation | | | |
| 1 hour | 90.2 | 63.3 | 76.1 |
| 2 hours | 80.7 | 59.8 | 73.2 |
| 3 hours | 73.0 | 50.7 | 68.1 |
| 4 hours | 60.0 | 41.4 | 66.2 |

* The splenic vein was connected to the inferior vena cava by means of a glass cannula through which had been threaded a piece of internal jugular vein. The portal vein and the hepatic artery were tied off.

TABLE 14—*Effect of Local Heat on Content of Dextrose in Blood and Skin, and of Glycogen in Skin, of Three Dogs (Average Determinations)*

| | Dextrose | | Glycogen in Skin,
Mg /100 Gm |
|---|----------------------|---------------------|---------------------------------|
| | Blood,
Mg /100 Cc | Skin,
Mg /100 Gm | |
| Control | 112.7 | 78.2 | 80.1 |
| After heating with stand lamp on one area | | | |
| ½ hour | | 85.6 | 80.1 |
| 1 hour | | 90.2 | 82.6 |
| Infra red lamp on another area | | | |
| ½ hour | | 92.1 | 81.6 |
| 1 hour | | 100.6 | 82.9 |

TABLE 15—*Influence of Phlorizin on Content of Dextrose in Blood and Skin, and of Glycogen in Skin, of Three Dogs (Average Determinations)*

| | Dextrose | | Glycogen in Skin, Mg /100 Gm |
|--|-------------------|------------------|------------------------------|
| | Blood, Mg /100 Ce | Skin, Mg /100 Gm | |
| Control | 112.6 | 71.7 | 77.6 |
| After phlorizin was given by mouth, 1 Gm daily | | | |
| 24 hours | 82.1 | 70.2 | 75.3 |
| 48 hours | 65.3 | 37.6 | 74.3 |

TABLE 16—*Effect of Application of Ice to the Skin on Blood Content of Dextrose and Cutaneous Content of Dextrose and Glycogen in Three Dogs (Average Determinations)*

| | Dextrose | | Glycogen in Skin, Mg /100 Gm |
|--|-------------------|------------------|------------------------------|
| | Blood, Mg /100 Ce | Skin, Mg /100 Gm | |
| Control | 102.8 | 74.6 | 69.7 |
| After ice was applied to skin and left there throughout length of experiment | | | |
| 10 minutes | | 60.7 | 68.7 |
| ½ hour | | 70.2 | 69.7 |
| 1 hour | | 80.7 | 69.9 |
| 1½ hours | | 82.7 | 70.1 |

TABLE 17—*Influence of Unfiltered Roentgen Rays on Content of Dextrose in Skin of Two Dogs (Average Determinations)*

| | Dextrose, Mg /100 Gm |
|------------------------------------|----------------------|
| Control | 88.6 |
| After application of 330 roentgens | |
| 24 hours | 85.8 |
| 48 hours | 87.3 |
| 96 hours | 89.5 |
| 1 week | 90.3 |

TABLE 18—*Effect of Exposure to Ultraviolet Rays from Cold Quartz Mercury Vapor Lamp on Content of Dextrose in Blood and Skin, and of Glycogen in Skin, of Three Dogs (Average Determinations)*

| | Blood Dextrose, Mg / 100 Ce | Skin | | | |
|---|-----------------------------|------------------------------|-------------------------------|------------------------------|------------------------------|
| | | Area 1 Dextrose, Mg / 100 Gm | (Right) Glycogen, Mg / 100 Gm | Area 2 Dextrose, Mg / 100 Gm | (Left) Glycogen, Mg / 100 Gm |
| Control | 106.2 | 76.2 | 69.7 | 78.7 | 70.8 |
| After irradiation for ten minutes with lamp 5 cm. from skin | | | | | |
| Immediately | | 75.1 | 69.8 | 77.6 | 70.4 |
| 20 minutes | | 80.1 | 69.6 | 78.9 | 69.7 |
| 40 minutes | | 90.1 | 70.1 | 78.7 | 70.2 |

RESULTS OF EXPERIMENTS

The intracutaneous injection of histamine caused the local cutaneous dextrose to rise and at the same time caused dilatation of the adjacent blood vessels. Contrariwise, the intracutaneous injection of epinephrine caused a decrease in the local dextrose and contraction of the blood vessels at the site. One explanation of this phenomenon is to assume a certain level of dextrose in the skin. This is an equilibrium point between the rate at which the skin disposes of dextrose and that at which it receives a supply. One factor governing the latter is the quantity of blood flowing past the skin site. If the blood vessels increase their size, as with the injection of histamine, and the skin's utilization of dextrose remains constant, then an accumulation of dextrose results. If the blood supply is reduced, as it is with the presence of epinephrine, then the dextrose at the site should fall if it is used up at a constant rate.

TABLE 19—*Effect of a Reducing Agent (Chrysarobin)* on Content of Dextrose and Glycogen in Skin of Three Dogs (Average Determinations)*

| | Right Side | | Left Side | |
|--|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| | Dextrose,
Mg /
100 Gm | Glycogen,
Mg /
100 Gm | Dextrose,
Mg /
100 Gm | Glycogen,
Mg /
100 Gm |
| Control | 80.2 | 72.1 | 79.6 | 74.6 |
| After application of 10 per cent chrysarobin ointment to right side | | | | |
| 10 minutes | 86.7 | 71.8 | 80.1 | 73.6 |
| 30 minutes | 93.7 | 74.2 | 80.2 | 75.6 |
| Control Skin excised from both sides and then chrysarobin ointment applied to right side | 76.2 | | 79.9 | |

* The chrysarobin was removed with ether and alcohol before the determinations of cutaneous dextrose were made.

This reasoning may explain the results obtained with the use of heat, cold, ultraviolet rays and reducing agents. Heat causes dilatation of the blood vessels and should cause a rise in cutaneous dextrose. Cold causes a contraction of the cutaneous vessels, followed later by dilatation. The dextrose first shows a fall followed by a rise. Ultraviolet radiation causes dilatation of the blood vessels, and in these experiments it raised the level of cutaneous sugar. It is probable that 10 per cent chrysarobin is sufficiently irritating to increase the blood coming to the site of application. Chrysarobin increases the dextrose. Whether such agents as ultraviolet rays, reducing agents, cold and heat have a specific action otherwise in relation to dextrose can be shown only by further work. Do they alter the rate of the consumption of dextrose in the skin? These experiments do not answer this or related questions. They simply point to quantitative results without explaining the mechanism of their achievement.

An attempt was made to follow the suggestion of Urbach and determine the amount of what he calls bound sugar, but the results were so variable that they could not be trusted. In such an analysis the skin is subjected to the action of strong acid in an attempt to separate the sugar from complex materials, presumably mostly proteins. It is impossible to know just what materials are obtained from such a violent reaction as that of strong acid on tissues. Undoubtedly reducing materials are yielded that are not carbohydrates. Urbach has not shown that they are indeed the latter. I feel that to reckon all these reducing materials as dextrose is an error. The source of some of them may be glycoprotein.

The determination of the contents of dextrose and glycogen in the skin when the latter is subjected to various kinds of agents and modalities helps one to gain an insight into the carbohydrate metabolism of the skin. It is impossible with the present data to get a nearly complete picture of the carbohydrate metabolism of the skin. Urbach claimed that this tissue has a peculiar carbohydrate metabolism of its own. He denied that the dextrose present in the skin is a mere diffusion product from the blood. He cited his observations that the amount of dextrose in the skin of some animals, such as the cat, was much higher than in the blood. I could not duplicate his results with animals. In all my experiments on various animals, I found that the skin contained slightly less dextrose than the blood or in some cases about the same amount. It is my belief that the dextrose present in the skin is a diffusion product from the blood. It seems quite evident from the present data that the skin is not a site for dextrose storage. The cutaneous sugar rises and falls with the blood dextrose after a very short latent period.

After the transfer of quantities of dextrose into the skin from the blood, an increase occurs in the cutaneous glycogen. An appreciable period elapses, however, during this conversion of dextrose to glycogen. The skin can hold the flood tides of dextrose from receding rapidly only if it converts it to starch. When the recession occurs, the glycogen slowly ebbs too, to a certain degree. The levels of glycogen and dextrose do not necessarily follow each other. Under the action of insulin the dextrose of the blood and that of the skin decrease, while the glycogen of the skin shows an increase. It is known that one of the actions of insulin is to aid in the synthesis of glycogen.

Phlorhizin poisoning causes a decrease in the dextrose of the blood and skin but no change in the cutaneous glycogen, as shown in the present work. The present belief is that phlorhizin interferes with the reabsorption of dextrose by the renal tubules. This results in a steady loss of dextrose through the urine, which is shown in the end

by changes in the blood and by the fact that the level of the cutaneous glycogen does not follow the lowering level of the cutaneous dextrose. Evidently the levels of the two substances can be independent of each other. It seems to be shown here, too, that cutaneous glycogen does not exist merely to furnish locally needed dextrose.

Just what the purpose or action of cutaneous glycogen is one cannot say at present. Apparently, it does not exist in the skin merely as storage material to furnish dextrose, as does the glycogen in the liver. If the liver is removed the blood sugar drops rapidly. The store of glycogen in the muscles and skin is considerable and could maintain the level of the blood dextrose for an appreciable time were it available for that purpose. If an animal is starved and the glycogen of the liver is depleted, it is found that the store of muscle glycogen decreases little. This points toward muscle glycogen having an action of its own apart from that of furnishing dextrose. It appears that the metabolism of glycogen in the skin follows somewhat the form it takes in the muscle and not that in the liver. Just how far the glycogen is utilized as a material independent of that of dextrose will be seen after further study. An aid in this direction will come from the oxygen and carbon dioxide analyses in respiration experiments on pieces of skin. It is my intention to conduct such studies.

The possibility should be considered that glycogen exists as a protecting substance. One of the modern beliefs is that glycogen is necessary for the protection of detoxifying processes in the liver. These processes may really be concerned with the mechanism of immunity. The skin is supposedly concerned with immunity, and it may be necessary to have glycogen present for this purpose.

These studies show that the more superficial layers of the skin contain more carbohydrate than the deeper ones. This fact is probably accounted for by the difference in the number of cells present in the respective layers. It would seem that the quantity of carbohydrate present depends on the number of cells present.

SUMMARY AND CONCLUSIONS

The literature on the carbohydrate metabolism of the skin is reviewed and discussed.

The dextrose content of the normal skin (excluding the subcutaneous fat layer) ranges from 60.2 to 81.5 mg per hundred grams.

The values for glycogen range from 68.1 to 84.7 mg.

There is a difference in the dextrose values found for the skin of different animals, but the amount in the skin is always related to the amount in the blood of the particular animal. The values for the blood are always greater than those for the skin.

The superficial layers of human skin contain more dextrose and glycogen than the deeper ones

The intravenous injection of dextrose causes sharp rises in the dextrose content of the skin but very minor ones in the glycogen content. The dextrose curve for the skin parallels that for the blood, with a lag in its rise and fall.

The injection of epinephrine for its systemic action increases the content of dextrose and of glycogen in the skin. The changes in the dextrose value are greater and more rapid.

The injection of insulin for its systemic effect decreases the dextrose content of the skin and increases the glycogen. The directional change of the values for dextrose and glycogen can be opposite.

If the circulation to and from the liver is effectively stopped, the dextrose in the skin decreases in time, while the glycogen is reduced relatively little.

Phlorhizin poisoning lowers the levels of blood and cutaneous dextrose but does not always affect the level of cutaneous glycogen. This again shows that the levels of cutaneous dextrose and glycogen can be independent of each other. Cutaneous glycogen does not exist merely to furnish locally needed dextrose.

The intracutaneous injection of epinephrine reduces the quantity of dextrose at that site and at the same time produces minor decreases in the glycogen content.

The intracutaneous injection of histamine increases the dextrose content at that site and changes the glycogen value very little.

The effect of the contact of ice with the skin is first to reduce the dextrose content of that part of the skin. Later, when the skin becomes congested, the dextrose content is increased. At the same time the glycogen value remains stationary.

Local heat to the skin increases the quantity of dextrose at that site with little change in the glycogen content.

Ultraviolet radiation without heat (cold quartz mercury vapor lamp) increases the dextrose in the irradiated skin without affecting that of the nonirradiated parts. The glycogen content is not changed.

Three hundred and fifty roentgens of unfiltered roentgen rays does not influence the dextrose content of the skin during the period of a week following such irradiation.

A reducing agent (chrysarobin) increases the dextrose of the skin on which it is applied but does not change the glycogen content during the period of half an hour.

The present work does not corroborate the concept of bound sugar. The foundations for this concept appear to need reexamination.

The dextrose content of the skin is dependent on that of the blood, dextrose is freely diffusible in the skin as well as in other tissues and organs.

The pattern for the use of glycogen in the skin seems to be similar to that in the muscle but not to that in the liver

Dextrose is not stored in the skin. Large additions of dextrose in the skin may be temporarily stored by conversion to glycogen. More work is necessary to discover the extent to which carbohydrate metabolism in the skin parallels that in the muscle. The indications of the present data are that it is somewhat similar in both.

ABSTRACT OF DISCUSSION

DR G V KULCHAR, San Francisco. I cannot agree entirely with Dr Cornbleet's interpretation of the data. Like most data, his are subject to more than one interpretation. There seemed to me to be several possible sources of error which I could not see rectified in his experiments. One is the use of anesthesia when the specimen is taken. Certainly his work shows that the local injection of vasoconstrictors and also the presence of vasodilators will alter the dextrose values. If he used no local anesthetic, I still would think that there was a possibility of the effect of emotional factors. Struggling by the animal will produce a considerable change in the dextrose content of the blood and also in that of the skin.

Another possible source of error which was not dealt with clearly in his report is the necessity of freezing the tissue immediately after removal. Certainly if the tissue is not immediately frozen there is the possibility of glycolysis and the conversion of sugar to glycogen.

It seems logical to explain all the results he obtained, particularly with the use of irritants, such as chrysarobin, ultraviolet rays, heat and cold, the last two of which have in the end the same vasodilator action, as locally injected vasodilators.

I cannot agree with him that the skin does not have an intrinsic carbohydrate metabolism of its own. Without going into too much detail, one of the things that leads me to this thought is that Dr Cornbleet maintains that the sugar simply pours into the skin and back again by a simple diffusion process. Several things lead me to believe that this may not be the case. One is that if it were a simple diffusion process, one would expect the dextrose curves of the blood and skin to parallel each other after the injection of a large amount of dextrose. As a matter of fact, they don't, there is a considerable lag. The second thing which leads me to believe that this may not be the case is the demonstration of the formation of lactic acid in the skin by Pillsbury. He has merely, as he said, scratched the surface of this problem. It seems to me that intimately bound up with these questions, and particularly when infections of the skin are concerned, is the relation of the increase in cutaneous dextrose to changes in the water content of the skin. Alderson and I have shown that there is an increase in water in the skin following an injection of a large amount of dextrose and that the effect of large amounts of dextrose on pyogenic processes, particularly in the skin, is due not to deposit of dextrose in the skin but rather to an increase in the water content of the skin.

DR M B SULZBERGER, New York. I am not competent to discuss this subject. However, Dr Sharlit, who should have opened this discussion, was unable to come. He asked me to say a few words presenting his views on Dr Cornbleet's contribution.

An even approximately correct understanding of the metabolism of the skin involves laborious and repeated efforts to establish the truth concerning the fundamental chemical units essentially implicated in that metabolism hence the inevitably repetitious reports on dextrose and glycogen in the skin of human beings and animals I consider Dr Cornbleet's contribution especially important because his findings are based on more adequate sampling than most of the work reported in this field Furthermore, I believe that he has supplied the most competent evidence yet available in substantiation of the contention that the dextrose concentration in the skin varies chiefly because of simple diffusion He has, with the same laboratory technic of analysis and by several approaches, established the fact that an increase in the size of the capillary bed in the skin (hyperemia) consistently tends to increase the concentration of dextrose And by the same token, his failure to influence materially the glycogen content of the skin under conditions of hyperemia corroborates the belief that diffusion alters dextrose concentrations

Using the same technic, Dr Cornbleet has observed that when any factor increases the local circulation of blood in a particular area, the dextrose in the skin of that area is also increased This observation is not, I believe, subject to Dr Kulchar's criticism of the possibility of error in technic

Whether or not dextrose and glycogen can be said to be stored in the skin is chiefly a matter of definition of the concept "store" Surely the concentration of dextrose in the skin tends to follow that in the blood, and when rapid depletion of the dextrose in the blood is accompanied by a slower loss from the skin, one might look on this lag as evidence of "storage" Definitely, glycogen is not stored in the skin in the same way as in the liver

Dr Cornbleet's suggestion that the time has arrived to correlate what is known about the carbohydrates in the skin with the respiratory quotient of the skin is so true that it may be said to be obvious

DR THEODORE CORNBLEET, Chicago I am sorry Dr Sharlit's illness prevented him from being here

The influence of anesthesia on the cutaneous sugar was studied There is a slight difference with and without anesthesia, whether it is general or local However, the conclusions from these experiments are not altered by this, inasmuch as all the values reported were found with the use of anesthesia, and the changes are all in the same direction The comparisons and correlations are therefore valid The conclusions drawn were controlled by results obtained without anesthesia

The emotion evoked by taking the biopsy specimen does not materially alter the values of the cutaneous sugar Even when considerable dextrose is injected directly into the blood stream, with enormous rise in the blood dextrose, there ensues an appreciable period during which no change occurs in the cutaneous sugar Any change in the level of blood sugar caused by emotion is far smaller than that induced by the injection of dextrose, with consequent parallel diminished effect on the skin Then, too, it required at the most four to five minutes to remove tissues for a biopsy, a period much shorter than the latent period required for the sugar level in the skin to follow that in the blood

The influence of the interval between the removal of the biopsy specimen and the determination of its sugar content was studied It was found that if the determinations were done within thirty to sixty minutes, little difference resulted when the skin remained at room temperature In the experiments just reported, however, chemical analyses were always begun soon after the removal of the skin

I agree with Dr. Kulchar that there is an intrinsic metabolism of sugar in the skin. I do not believe, however, that at the present time there is sufficient evidence to show that the skin has a special type of metabolism of sugar apart from that in all the other tissues. Lactic acid is present in the skin and probably comes from the glycogen. The mere presence of lactic acid, however, does not prove that there is a special type of metabolism present. Nor, in my opinion, would a parallelism in the sugar values of the skin and blood argue for a special kind of metabolism. If anything, that would indicate that the dextrose in the skin was there by diffusion from the blood.

I appreciate Dr. Kulchar's remarks in regard to the cutaneous sugar in pathologic conditions. I would rather not discuss that phase now, however, because the subject matter of the present paper includes only physiologic aspects.

THE "COMMON MOLE"

ITS CLINICOPATHOLOGIC RELATIONS AND THE QUESTION OF
MALIGNANT DEGENERATION

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This study was undertaken with the hope that some of the rather confused and apparently controversial ideas about moles (nevi) and their relation to cancer and melanomas might be made more readily and more generally understandable. Although the literature is replete with reports on the "common mole," there is little definitely known of its origin, development and relation to melanocarcinoma, because both clinical and histologic opinions on the comparative innocence or malignancy of a particular lesion are often widely divergent. This is discouraging from a practical point of view, as the observer is faced with the unpleasant prospect of a grave prognosis and many uncertainties as to the future course of treatment of what is probably one of the most common growths in the skin. A more positive knowledge of the development and ultimate fate of these lesions is, therefore, essential in order that their removal, which is often solicited for cosmetic reasons, may not be attended by aggravation of the condition or even more distressing results. It seems to us that in view of the complete and in many instances incomplete destruction of thousands of "moles" by various means, there ought to be more precise information concerning their final outcome, yet the present fund of knowledge is not only fragmentary but also confusing, owing to opinions based largely on uncontrolled clinical impression. The facts that the question has repeatedly been asked, "What is the 'common mole?'" and that we have found it necessary to begin our article with a definition of terms indicate the need to clarify the fundamentals of the subject. It is probable that if there

From The Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University

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Drs. David L. Satenstein, Francis Carter Wood, James Ewing, Frank Fraser, Elsie A. Barthel and S. W. Becker gave helpful opinions on questionable slides

were a uniform usage of accepted and clearly defined terms much difference of opinion would disappear and a clearer conception of the life cycle of the various marks which might come under discussion would be obtained. No two more unfortunate designations than mole and nevus can be imagined. From the beginning of this investigation it was apparent that a heterogeneous group of conditions was being included under the term mole, as used not only in the vernacular but also in medical parlance. In the first fifty odd lesions examined microscopically, there were eleven different conditions that had been designated clinically as the "common mole," and as the investigation was extended, other conditions were also found. Despite these difficulties, about 80 per cent of the first fifty lesions presented certain pathologic changes and, aside from minor variations in the anatomic features and certain differences in the gross clinical attributes, could be regarded as members of a single category. These lesions were characterized by the intracutaneous arrangement of nevus cells in typical configurations, such as nests, bands or strands. Kaiserling¹ pointed out that these remarkable collections of cells are recognized chiefly by their position and grouping rather than by their structure, which is variable. Though the appearance presented by these cells may vary a great deal, there is usually no difficulty in recognizing them, and they serve as the common denominator of a host of conditions for which such clinical terms as mole, soft nevus, cellular nevus and benign melanoma have been employed. Aside from the disadvantage of a multitude of names, some of the terms used are objectionable, though they enjoy the sanction of common usage, and it will be our endeavor to define these designations more accurately or give reasons opposing their employment in the nomenclature.

Nevus—The term nevus has been used to describe a circumscribed deformity (of the integument) of embryonal or evolutionary origin, which may be congenital or which may appear at any subsequent period during the patient's life.² This is a designation applied to a host of conditions seen at birth or shortly after. The English formerly restricted this name to the congenital vascular lesions, thus representing a usage that has not met with universal approval. The presence of the so-called nevus cells characterizes but one type of nevus for which we desire to restrict the designation mole or common mole. On the other hand, a type of lesion that we should like to call the potentially malignant melanoma may also occasionally appear early in life and therefore

1 Kaiserling, C. Naevi (Pathologische Anatomie), in Jadassohn, J. Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 2, pt. 2, p. 600.

2 Darier, J. A Text Book of Dermatology, Philadelphia, Lea & Febiger, 1920, p. 664.

may be classified clinically as a nevus, malignant changes in this type of growth should not be designated as nevocarcinoma for reasons that we will point out later. It is commonly observed that a single patient may show several or many varieties of nevi. These need not necessarily have the same origin, for example, there may be a so-called "common mole" on the face, Recklinghausen's disease on the trunk or/and an angioma on the limbs. In addition, several types of abnormalities may be found in a single growth, an example of which is shown in case 3. The term nevus, therefore, includes many types of lesions and of itself provides no clue as to the nature of the pathologic change to be expected. The designation pigmented nevus is a generic name applied to conditions having in common the occurrence of pigment, presumably melanin. The term pigmented mole, as commonly used, is a clinical designation applied to flat or raised lesions of various sizes and attributes, without implying anything as to the nature of the anatomic alterations. The expression nevus tardus, as it does not describe any specific type of mark and as many, if not the majority of, nevi are characteristically delayed in appearance or in development, is entirely superfluous, in our opinion.

Neuonevus—As the name indicates, neuronevus refers to a nevus arising from nerve tissue. In this sense, therefore, some of the lesions observed in Recklinghausen's disease may be designated as belonging in this category. The term neuronevus is sometimes applied to the "common mole," which in accordance with Masson's belief is regarded as originating from nerve elements. It is difficult to state at the present time what types of growths deserve to be placed in this category, but it is essential that all lesions labeled in this manner be demonstrated beyond cavil to be composed of nerve tissue or its derivatives.

Fibroma Molle, Soft Fibroma and Naevus Fibromatosus—These terms should be restricted to lesions characterized clinically by softness and pathologically by proliferating fibroblasts (connective tissue). There is a tendency for pathologists to diagnose such growths as neurofibromas, particularly if the cells are arranged in whorls. These growths, when situated on the face, may in some instances simulate the "common mole." The statement is often made that fibrosis represents an end stage of the ordinary mole, but our studies thus far afford no evidence favoring this view, although our material comprises lesions varying in duration up to thirty and forty years. It is possible that inflammatory fibrosis may occasionally be encountered in growths that have been traumatized, but this does not represent a true fibroma (case 7, possibly the report of case 6 may also be read in this connection).

Soft and Hard Nev—There are usually two general types: (1) the soft nevus, characterized by nevus cells in the cutis, by virtue of which the lesion is soft, and (2) the hard nevus, in which the essential altera-

tions reside in the epidermis. When the stratum corneum is thickened, the name keratoid nevus of Unna has been applied, when the layer of prickle cells is increased in thickness, the term acanthoid nevus has been used. Both layers may, however, be simultaneously affected, and the attribute of firmness is regarded as dependent on the pathologic changes in the epidermis. In a general way this division may be useful, but there are numerous exceptions and transitions. It is our belief that these clinical attributes cannot be employed as a means of classification. It may, however, be accepted that the pure hard nevus, affecting only the epidermis, has of itself no relation to the "common mole" or, probably, to the melanoma. In case 4 there was a lesion that was clinically firm, yet in addition to the epidermal changes, nevus cells were also found. The growth was the counterpart of the large pigmented lesions that are commonly called "bathing trunk nevi." Since the "bathing trunk nevus" has been described as occasionally having suffered malignant development, this case may be of interest from that standpoint.

Cellular Nevus—This term is applied to growths showing nevus cells, but as other types of congenital abnormalities in the skin may also reveal a variety of cellular collections in the cutis, there is a possibility that the meaning of this term may be distorted. The designation has less objection if it is understood to connote those lesions which contain only nevus cells as the pathologic criterion.

Mole—Unfortunately, popular usage has fixed the term *mole* in nomenclature. As it would be difficult to eradicate it and as it has been a source of confusion, it seems pertinent to define its meaning more precisely. By definition, then, the mole is regarded by us as a cellular nevus characterized histologically by the intracutaneous arrangement of nevus cells in special configurations (nests, bands and strands). Nearly all such lesions show the presence of a variable amount of melanin pigment both clinically and histologically, but this observation is not obligatory. These growths may be present at birth or appear shortly after birth or later in life. While an examination of our sections threw no light on the precise derivation of the nevus cells, there was, on the other hand, no definite evidence that the cells arise from the epidermis, as originally claimed by Unna.³ As will be shown, our studies thus far indicate that the "common mole" differs from the malignant or potentially malignant melanoma. This does not mean that the "common mole" and a malignant melanoma may not occur in different lesions in the same subject, as in a case under our observation, nor that a malignant melanoma may not complicate a preexisting intracutaneous mole.

³ Unna, P. G. Die epitheliale Natur der Naevuszellen, Deutsche Med.-Ztg. 18: 505, 1897.

which is an extremely rare occurrence but which we believe may have been taking place in case 15 (intradermal nevus in combination with an early nevus of the junction type) Authentic instances of the last-named combination are uncommon, when encountered, therefore, they should be recorded in the greatest detail Dr Satenstein has observed a number of such cases

Melanoma—The pigmented mole has been designated benign melanoma by some, for the purpose of contrasting it with the type of growth (malignant melanoma) that shows dangerous attributes, such as recurrence and metastases The distinction can be considered satisfactory only by those who regard the former lesion as a not uncommon precursor of the latter There are many observers who remain unconvinced that adequate proof of such transformation has been presented We are among those who consider the term objectionable as used in this sense Moreover, the medical public is apt to become overly uneasy when the designation melanoma is incorporated into any diagnosis, even if the prefix benign is appended, owing to the dissemination of much confused information as to the final outcome of such lesions It is our belief that the type of lesion giving rise to malignancy has features of a clinicopathologic order that permit differentiation from the "common mole" (see definition), though it is realized that this distinction cannot be easily established in every case We prefer to restrict the term melanoma to a lesion that is thought to be potentially or actually malignant It is true that a growth may be cancerous from the start, but there are numerous instances in which our present histologic methods are wholly inadequate to determine this point and the condition becomes evident only by the later course of events It is essential, therefore, to seek data based on other features, such as follow-up observations

By a potentially malignant melanoma we mean a lesion which has the ordinary clinical attributes of a growth known to become malignant if tampered with or situated at a site likely to be a source of chronic irritation but in which the pathologic study shows no apparent evidence of activity in the cellular elements or local spread at the time of examination and perhaps only slight evidence of a surrounding inflammatory reaction It is also requisite that the origin of the tumor be demonstrated as at the epidermodermal junction though for the present our studies do not justify any assumptions as to the exact nature of the cell in the lower layer of the epidermis which gives rise to the growth There is evidence that this origin is more easily demonstrable in the potentially malignant melanoma in which a secondary process, such as ulceration, hemorrhage or local growth, does not obscure this feature It is therefore essential to study sections from many portions of the lesion for the purpose of determining the primary site The potentially

malignant melanoma may be present from birth and hence may be designated clinically by some as a quiescent nevus or as a mole. There is evidence that such lesions may remain quiescent for many decades or even throughout life, especially if they are not exposed to trauma or other influences. It is, however, with such lesions that tampering, incomplete removal or chronic irritation is probably fraught with grave danger of active spread and metastases. We are still ignorant as to the incidence of such malignant change or the precise conditions under which this alteration takes place. The vast majority of such growths are smooth and devoid of hair, show a great variety of colors, including brown, blue and black, and usually are found on the extremities, especially the lower ones, though other sites, particularly the face, may also be affected. This is the type of lesion that may be diagnosed pathologically as benign and yet manifest itself later in the form of metastases, especially if incompletely removed. It is our belief that incomplete treatment of these growths by electrolysis, desiccation, coagulation or surgical removal is a dangerous procedure which may be followed by dire results. If our premises are correct, this type of lesion offers a hope of cure based on the complete prophylactic removal, provided metastatic foci are not present. While it is sometimes impossible to forecast whether metastasis has occurred, it may be put down as a cardinal rule that whenever the lesion shows suspicious characteristics or deviations from the normal (such as rapid increase in size, ulceration and bleeding), it should be removed widely. The growths that we have designated as junction type nevi represent what we consider potentially malignant melanomas (cases 10, 11, 12, 13, 14, 15 and 16).

Malignant Melanoma.—According to our views, the malignant melanoma is always a carcinoma, though the pathologic alterations may closely simulate a sarcoma in appearance. An advanced lesion of this type offers little hope for a complete cure except in variants which tend to run an exceptionally slow course. Such conditions require radical treatment in the hope that metastases, which may not be apparent, have not occurred or are of restricted distribution.

Nevocarcinoma.—This term should be applied only to that variety of growth in which these criteria are satisfied: (1) proof of the previous existence of true (intra-dermal) nevus cells and (2) proof that these cells have acquired cancerous properties. There are occasional observers who believe that the nevus cells do not undergo malignant change but that this complication occurs only in cells at the epidermo-dermal junction, the origin of the cells being unknown at present. Our observations are in accord with this view. It is our belief that such lesions are potentially or actually malignant melanomas, often superimposed on an ordinary intra-dermal mole, and that complication is

exceedingly uncommon. A biopsy specimen taken from one part of such a growth may show only the banal changes of the "common mole," yet another area of the same tumor may reveal alterations at the epidermodermal junction which we regard as the precursor of the malignant melanoma. There is reason to believe that when this combination occurs, the tumor presents distinctive characteristics. When such a change is suspected, incomplete removal or taking repeated biopsy specimens are procedures to be avoided. The label nevocarcinoma should not be applied to malignant pigmented growths merely because they arise from lesions existing at birth or in early life, for example, the pigmented marks seen on the soles early in life are regarded by us as the precursor of melanocarcinoma, and we believe that such lesions, if examined at inception, would show evidence of alterations at the epidermodermal junction. We have sought for lesions located on the lower extremities which might be catalogued as genuine intradermal moles, but our search thus far has been fruitless, it appears, therefore, that these regions are rarely the site of the "common mole" in the sense in which that lesion has been defined in this paper. This is an interesting and practical point, for the answers to our questionnaire clearly indicate that the vast majority of malignant pigmented growths have been found on the lower limbs. It may be argued that the "common mole" in this situation acquires new properties by virtue of the traumatic element to which it is constantly exposed, yet there were at least two points at variance with such a hypothesis. (1) We examined a lesion of relatively short duration (case 13) in which the pathologic changes were those of a junction type nevus or of a potentially malignant melanoma, (2) the factor of trauma is by no means negligible in the case of the ordinary mole on the face. Women frequently pluck hairs. A history of bleeding or infection in such growths is common. It is probable also that washing the face and rubbing with a towel several times a day cannot be considered a negligible source of trauma. Men frequently nick the lesions in shaving, and bleeding is not uncommon. Irritation may also occur in patients with a superimposed inflammatory eruption, as in acne vulgaris. Yet we have been unable to find a single lesion in which we could be certain that malignancy had supervened under such influences. In addition, we knew that innumerable such moles are incompletely removed because destruction of the cells below the level of the skin would result in a disfiguring pit. For this reason and because experience has shown that it is not dangerous to do so, we have not completely destroyed the base of such growths, and yet no untoward results have ensued.

Lentigines—The literature concerned with this subject is not only confused but also somewhat contradictory. Few observers are agreed on the clinical and pathologic nature of these lesions. Our material con-

tains too few examples to warrant a definite expression of opinion, yet a brief critical analysis may be useful. It appears that there are three types of lentigines

1. Superficial lentigines. The superficial variety simulates the ordinary ephelis, but it is differentiated clinically by its lack of definite relation to such external factors as exposure to sun and pathologically by evidence of epithelial proliferation in excess of that seen in ordinary pigmented spots, for example, those observed in Recklinghausen's disease. The peculiar epithelial proliferation appears to involve the cells in the epidermodermal junction, chiefly the so-called clear cells in the elongated pegs where the appearance of pale projecting bulbs is created. An example would be furnished in the case reported by Zeisler and Becker ⁴

2 Deep lentigines. The deep lentigines show more elevation clinically and a greater degree of activity at the epidermodermal junction. There is evidence of an inflammatory reaction in the cutis, although this may not be pronounced. An example of this type is furnished, in our opinion, in the case described by Ebert ⁵

The superficial and the deeper lentigines are usually multiple and generally occur in children. It is possible that the milder changes are susceptible of complete regression. It was recognized by Pollio,⁶ with whose opinion we are in accord, that the cells involved in the formation of lentigines are different from those seen in the ordinary intradermal nevus. It is our belief that the former lesions are probably potentially malignant melanomas, peculiar only in a number of clinical attributes. It is interesting that in the original presentation of Ebert's ⁷ case the following comments were made

In the very early lesion from which I secured a section there is a marked round cell reaction about the vessels around the lesion, and that is histologic evidence of the possibility of malignant change. Dr Jaffé looked at the section, and from what his associates said I understand that he considered the condition, histologically at least, as potentially malignant

3 Lentigo maligna. These spots are usually, but not necessarily, found in old persons, and their tendency to form cancerous growths is indicated by their name. We are of the belief that such lesions if examined at inception would show changes at the epidermodermal junction

4 Zeisler, E. P., and Becker, S. W. Generalized Lentigo. Its Relation to Systemic Nonelevated Nevus, *Arch. Dermat. & Syph.* **33**:109 (Jan.) 1936

5 Ebert, M. H. Multiple Pigmented Nevus. A Study of the Origin of the Nevus Cell, *Arch. Dermat. & Syph.* **37**:1 (Jan.) 1938

6 Pollio, G. Ueber Pigment-Naevi, *Arch. f. Dermat. u. Syph.* **80**:47, 1906

7 Ebert, M. H., and Wolf, M. J. Multiple Epithelial Nevus, *Arch. Dermat. & Syph.* **29**:765 (May) 1934, Multiple Nevus, *ibid.* **30**:292 (Aug.) 1934

analogous to the deeper types of lentigines seen in the younger age group. In all likelihood the melanotic whitlow belongs in this category or a related one. When Miescher⁸ wrote of melanocarcinoma as being derived from lentigines, he referred probably to lentigo maligna, and his several accounts indicated that he observed no essential differences between this type of malignant growth and that occurring on the basis of nevi. So-called lentigo maligna, in the opinion of Satenstein,⁹ is probably of two types, (1) the superficial junction type nevi and (2) seborrheic keratoses becoming malignant.

When these various types of growths show evidence of malignant change, it is erroneous to designate them as nevocarcinoma according to the criteria laid down in this paper, for it is our belief that these alterations do not concern the ordinary nevus cell as observed in the intradermal mole. There is a scarcity of evidence to indicate that the process of *Abtöpfung*, which in our opinion characterizes the potentially malignant melanoma, is the real source of nevus cells in the cutis, notwithstanding superficial resemblances, their common origin in early life and the rare instances illustrating a combination of both lesions. In agreement with the opinion expressed by Kaufmann-Wolf¹⁰ and others, the genetic process at the epidermodermal junction is regarded as potentially malignant (precancerous), whether it arises early or late in life. At present nothing is assumed as to the precise nature of this process, though the evidence appears to point to implication of the clear cells in the lower part of the epidermis, the relation to the so-called dendritic cells remains to be determined.

A second point that this investigation leads one to stress is the difficulty frequently encountered in deciding the differential clinical diagnosis between the "common mole" and the many small tumors of the skin with which it may be confused. As has already been mentioned, in the first fifty specimens studied there were eleven different growths that either had been or could have been confused with this type of nevus. A tiny nodular basal cell epithelioma certainly must cause frequent error, and this probably accounts at least for some of the reports of moles terminating in basal cell epithelioma. We have observed a number of cases of such an occurrence and included in our series is a patient who presented several lesions, of which one was desiccated as a "common mole" and another microscopically examined, proved to be a trichoeplithelioma (case 8). It is possible, though it no longer could be proved, that the lesion taken for a mole in this case might actually have been a

8 Miescher, G. Melanom, in Jadassohn, J. Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 12, pt. 3, no. 2, p. 1005.

9 Satenstein, D. L. Personal communication to the authors.

10 Kaufmann-Wolf, M. Beitrag zur Kenntnis der präcarcinomatösen Alteration bei pigmentierte Naevi, Arch. f. Dermat. u. Syph. 144: 73, 1923.

trichoepithelioma. As nevus cells were not found histologically in any of the growths which proved to be epitheliomas, we cannot assume that in our cases such a transition actually took place. Other conditions, further illustrating this diagnostic difficulty, are described in the detailed classification of our cases.

Before undertaking this investigation, we felt that it would be useful to have an expression of opinion on certain points from a group of American dermatologists as a basis for future comparison. A questionnaire was therefore submitted to about one hundred and twenty members of the American Dermatological Association. The questions proposed were: 1. Have you ever seen a small common hairy mole become malignant? 2. Have you ever seen a histologically proved benign cellular nevus (mole or pigmented mole) become malignant subsequently? The data furnished on the basis of ninety-three answers not only proved interesting but reflected the confusion of ideas attending this subject, hence a brief analysis of them appears warranted. Of the ninety-three dermatologists, eighty-five had not observed malignant change in a small common hairy mole, despite manifest opportunities to witness such transformation. In addition, this group has never seen a histologically proved benign cellular nevus (mole or pigmented mole) become malignant subsequently. It is realized that biopsy specimens are rarely taken in such cases in private practice and that this procedure is more commonly carried out in dispensaries and hospital services. It is important, therefore, that of the dermatologists in this group, many had access to a tremendous amount of pathologic material. When it is further considered that many of these lesions have been subjected to daily irritation or to the trauma of complete or incomplete removal, these statistics are most noteworthy. The statistics supplied by the questionnaire, which was apparently correctly understood, completely refute the erroneous idea generally prevalent that the "common mole" is attended not infrequently by cancerous degeneration. The result of the examination of the numerous specimens comprising the basis for this report entirely substantiates the idea of the exceedingly great rarity of cancer as a complication or sequel to the "common mole" (intradermal nevus).

The few members who reported a change to malignancy described growths that were smooth, bluish black or steel blue, devoid of hair and generally situated on the extremities, especially the lower. One observer mentioned a case in which the lesion occurred on the arm and contained a few tiny hairs but in his opinion "This was not a true hairy nevus in the accepted sense." Another stated that in his experience the blue-black or steel blue mole was the precursor of malignant melanoma, yet he added that in his opinion "The common practice of pulling out hairs from the ordinary pigmented nevus or the occurrence of slight secondary infection from a variety of causes might stir up such a lesion." He

was, however, willing to admit that the constant nicking, as in shaving over his own moles, had not been a competent producing cause. These observations seem to illustrate one of the common inconsistencies prevalent, for the blue-black or the steel blue growths which are generally accredited with developing into the metastasizing melanoma are lesions usually devoid of hair, certainly of coarse hair. While pigmented nevi with hair (the hair being an essential part of the nevus) may under exceptional circumstances produce malignant melanoma, the occurrence appears to be rare. Another observer expressed the belief that the pigmented hairy nevus might become malignant, but only in the same sense that normal skin might become cancerous after chronic irritation—a viewpoint becoming more and more generally accepted. A few had seen clinically benign pigmented lesions undergo malignant change, but it is our surmise, from the few details furnished, that they were the smooth brown, bluish black or slate blue growths and, perhaps also, the rare relatively nonpigmented melanoma. Others, noting the same sequence of events, were doubtful that such lesions had been benign from the beginning in the pathologic sense (Brunsting). On the other hand, one observer had encountered conditions diagnosed as malignant on the basis of microscopic examination (we do not know whether a dermatopathologist or a general pathologist was responsible for this opinion), yet clinical observation appeared to indicate that the growths were benign. This occurred repeatedly in our series also, and not infrequently three or four outstanding dermatopathologists differed in opinion. In an isolated instance mentioned in another reply to our questionnaire, half the lesion appeared benign, whereas the remainder was malignant. A follow-up letter asking for further details failed to supply a complete clinical description of the case together with the pathologic changes present on which the diagnosis of malignancy was based. At the other extreme was the following statement made by one of the physicians, "Most of the fear of malignant degeneration following removal by coagulation or desiccation is either pure hysteria on the part of misinformed general practitioners or propaganda on the part of the surgeon who wants to excise these growths." In perusing a complex literature, especially that found in surgical journals, it is evident that surgeons as a group have contributed greatly toward the confusion. A notable exception is Affeld's paper,¹¹ which is based on a clinicopathologic correlation; it is interesting that in a study of 266 instances of malignant melanoma he did not encounter a single example arising from a hairy mole.

What determines the change from a benign to a malignant process? Is it trauma? Or does trauma play only a minor role, the essential

11 Affeld, D. H. Melanomas, *Am J Cancer* 27 120, 1936

motivating factor being unknown? In the development of malignant melanoma, trauma without a doubt is the precipitating factor in some of the cases, the exact percentage of which it is most difficult to determine, as the point hinges somewhat on the reliability of the history or on supposition or theory. Trauma is credited with playing a part in a number of cases reported by Gleave, Amadon, Coley and Hoguet, Stevenson, Hazen, Farrell, Klauder and others¹². More than 50 per cent of the conditions occurred on the feet, which in itself is somewhat suggestive. The next most common site, the head, is also a part particularly liable to injury.

In many of the specimens that were studied, considerable difference of opinion arose as to whether the process was benign or malignant. For instance, if "trickling off" (*Abtropfung*) and segregation are essential alterations that may be seen in either a benign or a malignant lesion, it may not be unreasonable to suppose that the factors responsible for these phenomena in a benign mark may, through local irritation or stimulation, be changed to give rise to a malignant one. Some vital agent must still be discovered, however, to account for subsequent events, namely, extension of the tumor, metastasis or the occasional rare regression or complete spontaneous disappearance of growths, such as have been recorded in the literature.

Kreibich¹³ described a case of melanotic nevocarcinoma combined with melanotic lymph gland tumor in a man of 50. The nevus itself was not affected by the tumor. Histologically, extensive degeneration of the epithelium with "trickling" (Unna) of the epithelial cells into the cutis was found. The author distinguished two forms of epithelial "trickling," a benign one, as in nevus, and a malignant one, as in melanocarcinoma. The relation to Paget's disease was mentioned. He called attention to the fact that simple pigmented nevi (i. e. smooth, nonwarty and nonhairy) were more disposed to the development of carcinoma than were cellular pigmented nevi (intra-dermal nevi), a point that we wish to emphasize.

The exact significance or correct interpretation of epithelial "trickling" is therefore of the greatest importance, not only from the standpoint of the origin of nevi but from the point of view of malignant activity as well. According to Miescher,⁸ "trickling off" occurs slowly and only in a few small areas in nevi, so that it has to be looked for diligently; but in malignant melanoma it forms the principal element of the picture. Our so-called junction type nevus (group 3 and figs

¹² Farrell, H. J. Cutaneous Melanomas, *Arch. Dermat. & Syph.* **26** 119 (July) 1932.

¹³ Kreibich, C. Ueber Naevuscarcinom, *Arch. f. Dermat. u. Syph.* **130** 542, 1921.

12 to 20) can be recognized by the "tickling off" of cells and also by the presence of the clear or embryonic cells, which may resemble the Paget cell and which represent probably changed epidermal cells. Great difference of opinion exists as to the origin of the cells.

It is interesting to note that our group of junction nevi seem to fall into two categories: (1) those in which the original lesion is observed early in infancy (congenital) and (2) those in which the mark appears about puberty or in adult life. In our collection of cases the latter type was more common, and, in addition, the lesions were of comparatively recent origin, i. e. two months, three months, six months, three years and six years, respectively, in 5 of our cases (not to mention others). In adults showing lesions of such short duration, the question arises whether they should be considered as of nevus origin (hence, originally benign). Microscopically the lesions showed changes apparently indistinguishable from those seen in the first (congenital) group, in which the factor of trauma or irritation seemed to play an important part in their further development. It appears, then, that the histologic characteristics cannot be used as the sole criterium for determining origin or prognosis. The apparent difference in frequency of occurrence and prognosis between the congenital and the delayed or acquired types of junction nevi has been noted also by Pack,¹⁴ who "in a careful clinical investigation found that the average person has at least twenty pigmented spots. These spots are important because they may cause disfigurement or become malignant. Five patients with undoubted congenital nevocarcinoma were alive and well without recurrence of the condition, 2 for five years, 3 for two years and 1 for one year after treatment. Of the 20 with acquired conditions, 15 were dead. While we consider the junction type nevi as potentially malignant it would appear, from our observations, that like other so-called precancerous lesions they need not necessarily terminate in malignant melanomas. This is true at least for the relatively short time we have been able to keep our patients under observation and seems to be particularly the case with marks of the congenital junction type, the latter having therefore a much better prognosis.

Unna³ many years ago called attention to a phenomenon in the epidermis overlying nevi, namely the appearance of cavities containing free epithelial cells. Unna stated the belief that these free cells gradually find their way to the cutis (*Abtöpfung*), where they are transformed into nevus cells. Darier¹⁵ found this phenomenon in two

14 Pack, cited by Adair, F. E. Treatment of Melanoma. Report of Four Hundred Cases, Surg., Gynec. & Obst. 62:406, 1936.

15 Darier, J. Des naevocarcinomes, Bull. Assoc. franç. p. l'étude du cancer 6:145, 1913.

of nine nevi and in nine of nineteen primary nevocarcinomas. He called these collections of cells *thèques*. He definitely stated that they were present only in the primary tumors.

Nicolau¹⁶ recently contributed his own observations on a case of nevocarcinoma with numerous metastases. In a number of these metastatic tumors, he found in the more advanced masses and occasionally in the hair follicles and rete pegs some cavities (*thèques*) containing larger or smaller numbers of free cells showing no intercellular filaments. From these results, Nicolau argued that the original conception of Unna of the role of these free cells in the genesis of nevi and nevocarcinoma must be revised. He stated the belief that the free cells originated from the tumor and were in reality an intraepidermal metastasis. From a study of the histologic preparations, it appeared that the cells reached the epidermis one by one and by division formed a small mass, which was finally extruded by normal exfoliation.

Darier,¹⁷ commenting on the aforementioned statement of Nicolau, stated the belief that there was no question but that the histologic changes noted by the latter were identical with those noted in primary tumors by Darier. Nicolau, however, laid no stress on certain changes in the cells of the basal layer which to Darier were of capital importance, since they were in his opinion the starting point of the entire process. Hence he rejected Nicolau's conception of a migration of neoplastic cells into the epidermis. In Darier's opinion, the close approximation of the neoplasm caused changes in the basal cells which led to the formation of *thèques*. This seemed the most plausible explanation of the process, though admittedly it was purely hypothetical. Recently Becker,¹⁸ Satenstein and others have stressed the epidermodermal junction as the probable starting point of the process. This appeared to be true of the specimens we studied, especially as our series included only those lesions which were considered to be early.

CLINICAL AND PATHOLOGIC CLASSIFICATION

As stated previously, about 80 per cent of the marks examined in our series fitted into the category characterized by the arrangement of nevus cells intracutaneously in nests and strands. Histologically this represents the type that has been designated as the intradermal nevus.

16 Nicolau, S. Sur le phénomène de migration cellulaire intra-épidermique dans le naevocarcinome (à propos de l'étude des tumeurs de métastase), *Ann de dermat et syph* 1:746 (July) 1930.

17 Darier, J. Note sur les cellules du naevocarcinome. Leurs migrations et leurs propriétés cancérogènes (à propos du mémoire du Prof Nicolau) 1:763 (July) 1930.

18 Becker, S. W. Cutaneous Melanoma. A Histologic Study Directed Toward the Study of Melanoblasts. *Arch Dermat & Syph* 21:818 (May) 1930.

The "common mole," according to our conception, is one of several examples of an intradermal nevus. It is unfortunate that the intradermal nevus has so many varied clinical types. This type of nevus exceedingly rarely gives rise to cancer or to malignant melanoma. If the malignant condition occurs, which is exceptional, it is probable that the nevus is not a pure intradermal type but represents a combination referred to in group 4.

As moles (nevi) must in the last analysis be classified on the basis of their histologic structure, the following classification is suggested:

1 *Intraepidermal Nevus*. This is essentially a clinical type, as histologically no nevus cells are found, and only the history and clinical picture suggest its nevus origin. Marks which may be clinical examples are

- (a) *Naevus verrucosus* (hard warty nevus)
- (b) *Naevus verrucosus linearis* (linear warty nevus)
- (c) *Naevus papillomatosus* (a bad designation, as it probably generally refers to a soft warty nevus, which would place it in group 2)

2 *Intradermal Nevus*. Marks which may be clinical examples are:

- (a) *Verruca mollis*, soft wart or cellular nevus (the "common mole")
- (b) *Naevus papillomatosus* (group 1)
- (c) *Lentigines*, deep (?) (the so-called beauty mark seen frequently on the face)
- (d) *Naevus pigmentosus et pilosus* (pigmented mark with hair)
- (e) *Naevus pigmentosus et verrucosus* (soft warty pigmented mark)
- (f) *Naevus pigmentosus et pilosus et verrucosus* (combination of pigmented hairy and soft warty mark)

3 *Junction or Borderline Nevus*. Marks which may be clinical examples are

- | | | |
|---|---|--|
| <ul style="list-style-type: none"> (a) <i>Naevus spilus</i> (small smooth flat pigmented spot) (b) <i>Naevus pigmentosus</i> (c) <i>Lentigines</i> { (1) superficial
(2) deep (d) <i>Naevus pigmentosus et verrucosus</i> (exceedingly rare, when it occurs it may represent a combination type [case 15]) (e) <i>Naevus pigmentosus et pilosus</i> (exceedingly rare) | } | <p>Clinically may be indistinguishable from those which microscopic examination would place in another group</p> |
|---|---|--|

4 *Combination Type Nevus*. Histologically it exhibits a combination of one or more of the three types already mentioned. Clinically it assumes the characteristics of one or several of the previously mentioned varieties.

5. *Blue Nevus* This, fortunately, is a histologic as well as a clinical designation. Clinically the mark is probably often mistaken for a slate black mole (malignant melanoma)

A brief description of the histologic classification seems necessary

1 Intraepidermal nevi lie entirely within the epidermis and present a proliferation of normal epithelial cells, a mixture of prickle and basal cell type, not referred to as nevus cells. They may or may not be pigmented. They rarely terminate in cancer.

2 Intradermal nevi are probably the most frequently encountered lesions and are characterized by the occurrence of nevus cells arranged intracutaneously in nests and strands. The cells are of the mature type, and to become malignant they revert to the embryonic type. Pigment is generally present in varying amounts. Cancer or malignant melanoma rarely, if ever, occurs.

3 In junction type nevus (Satenstein) or borderline melanoma Becker¹⁸ stated "The process may be interpreted as hyperpigmentary due to an increased number of melanoblasts at the epidermo-dermal junction." The cells are not separated from the epidermis as in the intradermal nevi, in which the nevus cells are seen in nests or strands usually detached from the epidermis. The cells in this type are of the embryonic (anaplastic) type, and the lesion constitutes the forerunner of the malignant neoplasm. It is the lesion we prefer to call the potentially malignant melanoma. The criteria necessary to decide whether a junction nevus has definitely become a malignant melanoma require careful consideration of both the clinical picture and the course of the lesion, as well as a minute study of the histologic changes. Lesions are encountered which clinically seem innocent and which apparently pursued a benign course as long as we have been able to keep the patient under observation. But the reports on slides studied in these cases by various pathologists show great differences of opinion. If a report of malignant melanoma had been accepted in such cases without due consideration of the innocent clinical course, great harm might have been done. We believe that the clinical criteria for malignant melanoma have been sufficiently stressed so that it would be superfluous for us to restate them, but the histologic grounds or basis for such a diagnosis certainly seem less clearcut.

It appears logical that the following points are necessary for the diagnosis of malignant melanoma: (1) "trickling off" and segregation (development of *thiQUES*) (one of the principal changes and found without difficulty), (2) the presence of clear cells, which may resemble the Paget cells, (3) mitotic figures (generally readily found), (4) variably sized and shaped (large and small) pigment cells and (5) chronic inflammation. The more evident each of these changes appears in the section, the more certain one may be of the malignant nature of the growth.

4 The combination type nevus represents a combination of types 1, 2 and 3 (case 15).

5 The blue nevi (slate blue or grayish blue), which are chiefly found as isolated lesions on the face and dorsum of the hands, have no relation to melanoma. The color is apparently determined by the number and depth of the melanoblasts. It must be emphasized that the name blue nevus should be restricted to pigmented growths composed of a peculiar type of connective tissue cells apparently capable of forming melanin, that so far as the literature and our limited observations are concerned these spots are benign in their course, and that diagnosis on the basis of color alone is unreliable, as other lesions, such as the melanoma and the

"common mole," may reveal similar shades of blue. In rare instances¹⁹ an ordinary intradermal mole may show clinical features apparently indistinguishable from those of the blue nevus, this phenomenon is apt to occur when the nests of nevus cells and their accompanying pigment are separated from the epidermis by a wide stretch of intervening connective tissue. It is interesting that a number of cases have been recorded in which the characteristics of an ordinary mole were associated more or less intimately with those of the blue nevus of Tieche.²⁰ This represents another example of a combination of nevi. It has been claimed that blue nevi may terminate in sarcoma, but such a change must be rare indeed, for Satenstein,⁹ Becker, Peck, Ewing, Wood and Fraser²¹ have not seen examples of it.

In our studies we included only 1 case of intraepidermal nevus, since this type was not related to the "common mole" or to the melanoma. Case 1, in which the growth typified the intraepidermal nevus, should, however, be recorded, because in one portion of the section the epidermis appeared to be invading the cutis, and it was Dr. Satenstein's belief that this represented an early stage in the formation of squamous cell epithelioma, which was the type of transformation to be expected in intraepidermal nevi. However, intraepidermal nevi are rarely complicated by cancer, this case being an exception rather than the rule.

REPORT OF CASES

CASE 1—M. K., a woman aged 37, had had a lesion on her right cheek for the past nineteen years. In the past two years it had attained the size of a large pea. The growth was somewhat pedunculated, light brown, moderately firm and definitely verrucous. In the center there was a dried hemorrhagic crust, the probable result of recent trauma. The lesion was removed and the base desiccated. Healing was uneventful.

On microscopic study the chief changes were observed in the epidermis, all of its layers being hypertrophied. There was decided hyperkeratosis, which followed all the irregularities in the surface of the growth. At the point corresponding to the central hemorrhagic crust were areas of parakeratosis disposed unevenly and amorphous masses that probably represented the remains of old hemorrhage. There was decided acanthosis, and the basal membrane was intact except for a small area where the cells seemed to be penetrating the cutis. The lower layers of the epidermis showed moderate intercellular edema, scattered areas of intracellular edema, rare mitotic figures and a few leukocytes. In the immediately adjacent cutis there was a chronic and acute inflammatory reaction composed mainly of blood vessels, perivascular lymphocytes and a few polymorphonuclear leukocytes, in other areas there was a conspicuous increase in the number of blood vessels and fibroblastic cells, as observed in chronic granulation tissue.

The diagnosis was intraepidermal (hyperplastic) nevus with a lesion that apparently was an early stage squamous cell epithelioma.

19 Sato, K. Beitrag zur Kenntnis des "blauen Navus," *Dermat. Wchnschr.* 73: 1073, 1921.

20 Tieche, M. Ueber benigne Melanome (Chromatophorme) der Haut, "blaue Naevi," *Virchows Arch. f. path. Anat.* 186: 212, 1906.

21 Becker, S. W., Peck, S. M., Ewing, J., Wood, F. C., and Fraser, J. F. Personal communication to the authors.

CASE 2—L O, a woman aged 47, was observed April 15, 1936. There were two lesions on the face. The one on the left cheek had been present during her entire life. It was sessile, pea sized, fairly smooth and moderately firm and showed a mottled brown surface with many fine telangiectases. On several occasions it had bled after injury, but the precise nature of the trauma could not be ascertained. This growth was known to have antedated the appearance of the one on the opposite cheek, the latter having been present for some thirty-five years as a

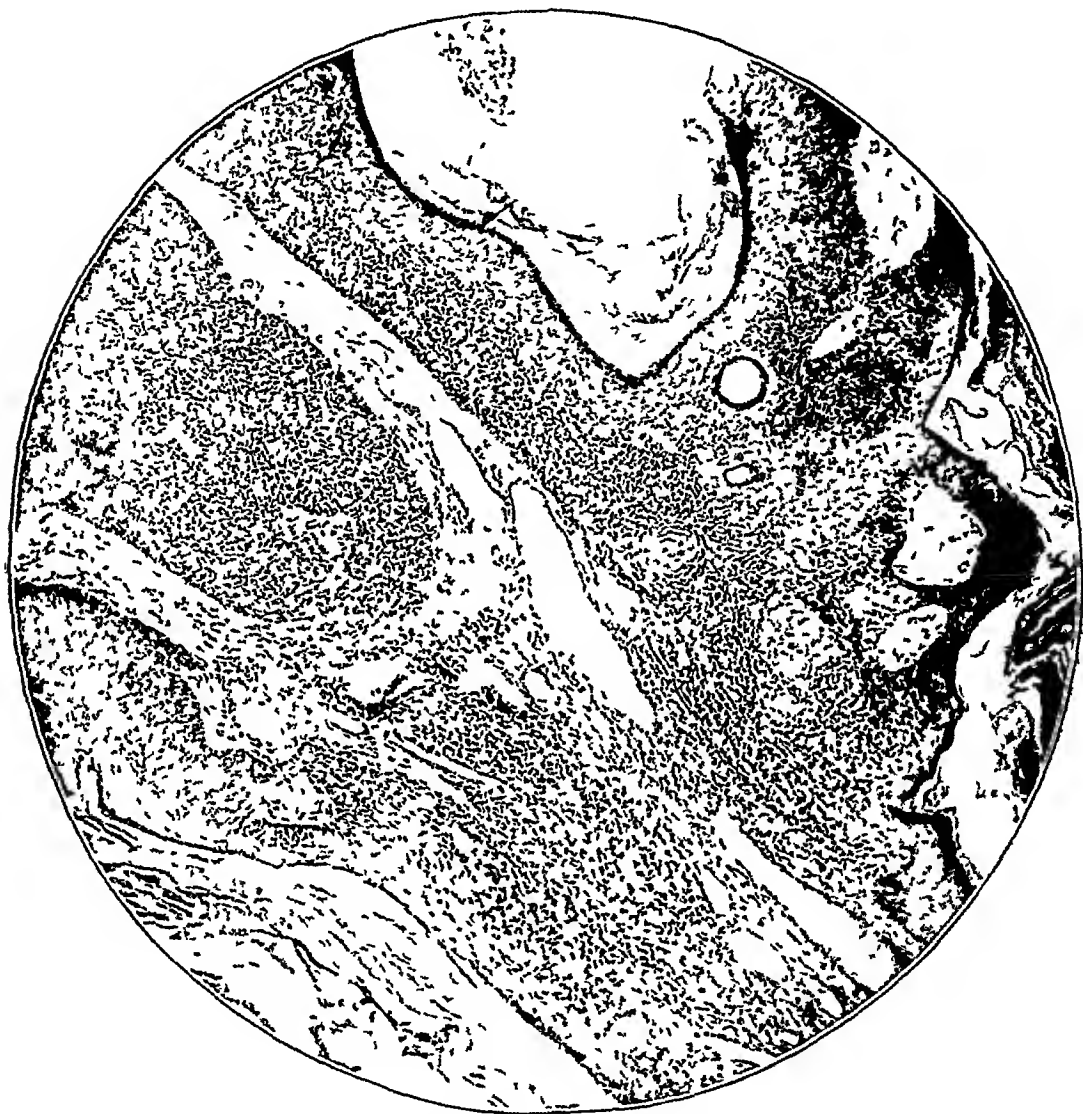


Fig 1 (case 1)—Intraepidermal (hyperplastic) nevus with what appears to be an early squamous cell epithelioma

slightly smaller lesion which was moderately firm and the color of normal skin, with a definitely yellow overtone. Both growths had always been devoid of hairs, and in both an increase in size had occurred gradually.

The diagnosis was intradermal nevus.

Histologic examination of the growth on the left cheek (fig 3) disclosed the typical changes of the "common mole." The epidermis was thin. The zone of nevus cells was separated from the epidermis by a layer of connective tissue containing many dilated capillaries. There were scattered deposits of pigment



Fig 2 (case 2) —Two “common moles” of different size and color



Fig 3 (case 2) —Low power section of the intradermal nevus on the left cheek

chiefly at the upper limit of the cellular infiltration. The nevus cells were arranged in typical groups, nests and strands. The sebaceous glands were relatively few or in a definite atrophic state, a condition that seemed to be caused by the mechanical pressure of the masses of nevus cells. There were a few hair follicles.

The minute anatomy of the lesion on the opposite cheek was essentially similar except that there were more sebaceous glands, which appeared to be fairly normal. It was our impression that the presence or absence of these structures may have played a part in determining the color of the growth by adding a bulk of sebaceous matter to the lesion.

CASE 3—A D, a girl aged 14, was born with a small spot on the upper lip. The mother did not remember the color of the growth at birth, but hairs had always been present. It had grown slowly, reaching its present size about four years ago. The lesion extended from a point near the vermilion border of the upper lip to the left nostril. It was dime sized, pinkish brown and raised several millimeters above the level of the normal skin. The surface was irregularly pitted, and numerous hairs were present, many being coarse.



Fig 4 (case 3)—A pigmented warty and hairy nevus fulfilling the requirements of the "common mole"

The diagnosis was intradermal nevus, with lymphangioma.

Microscopic examination showed masses of nevus cells throughout the upper and middle part of the cutis in the form of groups, nests, bands and some strands. The epidermis showed only thinning, probably due to the mechanical pressure of the infiltrate, and depressions corresponding to the follicular openings, the latter seemed to explain the clinical resemblance to an orange peel. Between the epidermis and the masses of nevus cells, there were greatly dilated epithelium-lined spaces. These, because they did not show the presence of red blood cells, were regarded as lymphatic channels (lymphangiectases), it is possible, however, that they were originally blood channels of congenital origin. The masses which were found in the major part of the cutis were composed of uniform cells showing small darkly staining nuclei, without visible cellular outlines. Pigment was not found in these sections, but its occurrence was noted occasionally when the studies were made only with the hematoxylin and eosin stain.

CASE 4—On the upper part of the right arm of a girl of 16 there was an oval hairy and verrucous blackish brown lesion. It measured $1\frac{1}{2}$ by 1 inches.

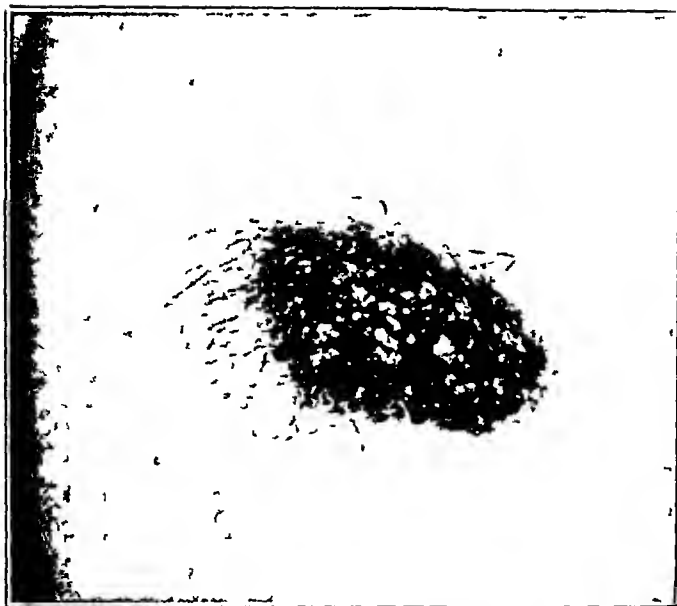


Fig 5 (case 4)—Pigmented warty and hairy nevus ("common mole")

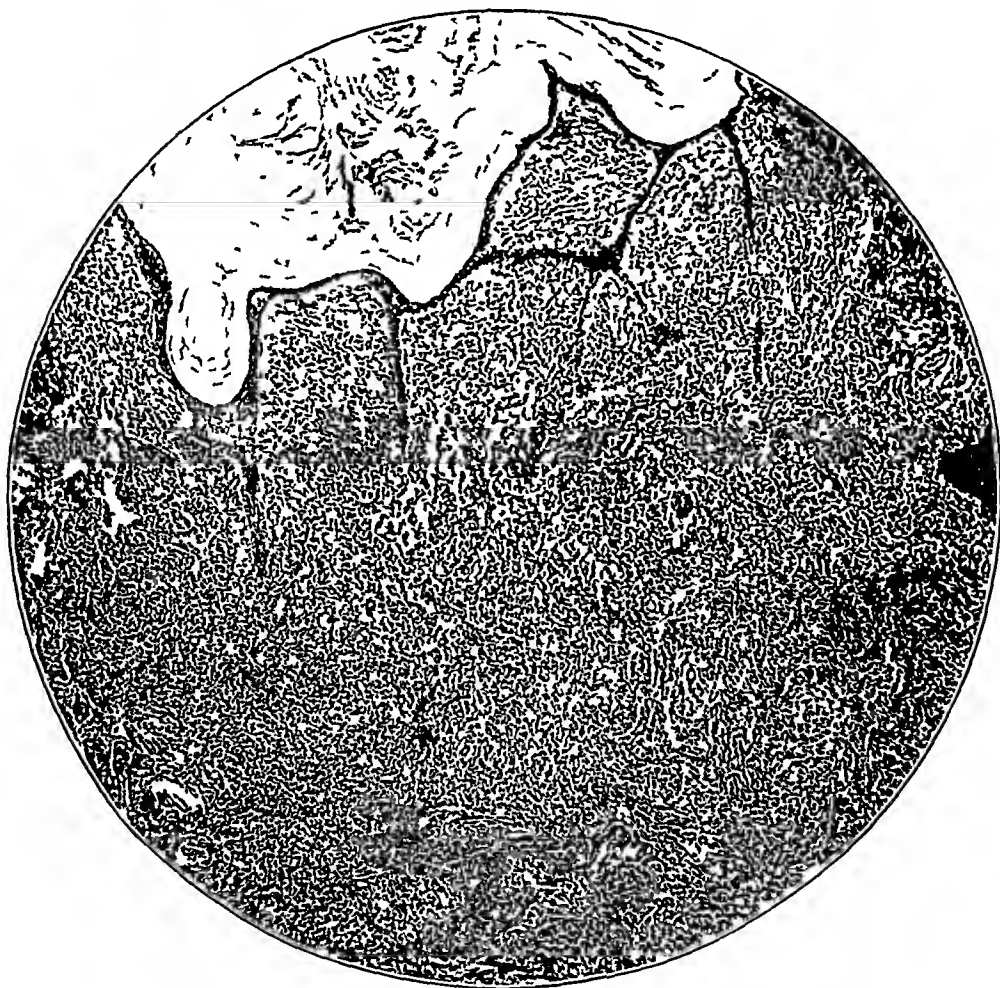


Fig 6 (case 4)—Low power section of verrucous intradermal nevus

(3.8 by 2.5 cm) in the longest diameters. The numerous hairs were black and coarse. The growth had been present from birth and had gradually increased from a small spot to its present size. The patient believed, though she was not certain of the point, that the hairs had appeared only during the past seven or eight years. With the area under local anesthesia the lesion was excised, and the wound healed in two weeks.

On histologic examination the epidermis was found to be thrown into many papillomatous folds, due to the collection of edematous nevus cells. There was a thick hyperkeratotic scale which was responsible for the hard part of the lesion. The remainder of the epidermis was atrophied owing to the pressure of the masses of nevus cells. In many places there was a definite layer of connective tissue that separated the thinned epidermis from the groups of nevus cells and in intervening areas occasional clumps of pigment. There were many hair follicles which had



Fig. 7 (case 5)—Verrucous intradermal nevus. The rounded smooth mass near the upper center is a large hematoma that had been mistaken clinically for an early melanocarcinoma.

been cut at various angles. The nevus cells were diffusely arranged down to the deeper layers of the corium in the typical manner observed in an ordinary mole.

The diagnosis was verrucous intradermal nevus.

CASE 5—A. Z., a woman aged 29, presented a naevus pigmentosus et pilosus et verrucosus of the elbow, the growth having been noted at birth. The large round smooth mass which looked like an early malignant melanoma developing on the original nevus was seen to be a hematoma on microscopic examination. This case illustrates a not infrequent clinical error.

The diagnosis was verrucous intradermal nevus with hematoma.

CASE 6—S. C., an Italian woman aged 54, had a single growth on the left ala nasi of nine years' duration. It had apparently arisen on normal skin as a pimple, which had grown gradually to attain a length of almost 1 inch (2.5 cm) and a breadth of $\frac{1}{2}$ inch (1.3 cm). The mass was soft and slightly lobulated and hung from a slightly constricted pedicle. The surface was mottled in appearance, in areas it had the color of normal skin, with interspersed dull white depressed spots.

creating the effect of fine lobulations, in other areas it was reddish and bluish, with superficially coursing telangiectatic vessels. The growth was soft to moderately firm on palpation. There had never been any growth of hair, and it had bled frequently, especially when traumatized, as in the act of washing the face. It was removed by an elliptic incision, and the base, which bled freely, was cauterized.

On histologic study the epidermis was found to be thin, with a decided amount of pigment in the basal cell layer. The growth consisted of an edematous stroma containing many new blood vessels and lymphatic spaces. Occasional hair follicles were encountered at one edge of the specimen, but no collections of nevus cells.

It was the opinion of Dr. Sateuism that the lesion was an angiosarcoma. Several other pathologists regarded the lesion as a pedunculated fibroma. The histologic features were sufficiently unusual that a final diagnosis could not be given except to state that the growth was not a nevus despite its rather close clinical resemblance to the "common mole."



Fig. 8 (case 7)—Clinically this lesion was looked on as a "common mole," but on histologic examination was proved not to be intradermal nevus.

CASE 7—Since birth, this patient, a man of 23 years, had had a small elevated pea-sized circumscribed nodule located at the root of the nose. The lesion had a peculiar dull white color, the paleness being accentuated by a surrounding group of minute comedos. The growth was firm, smooth and devoid of coarse hairs. There was no history of bleeding or of trauma.

Histologic examination showed that the epidermis was relatively normal. There were occasional prolongations of the rete pegs, which probably represented cross sections through the hair follicles cut on the bias. There were many clear cells in the basal layer of the epidermis and of the hair follicles, but no definite deposition of pigment. In the upper part of the corium there were numerous blood vessels. Scattered throughout the cutis there were many sebaceous glands, hair follicles and sweat glands. The upper half of the cutis contained an infiltration of what appeared to be typical fibroblastic nuclei, and the superior portion of the infiltrate showed scattered connective tissue cells containing pigment, the pigment was chiefly arranged in the form of fine granules, though some of it was also deposited as irregular masses. Van Gieson's stain revealed that the groups of fibroblast-like cells had but little intercellular substance taking the pink color of connective tissue. The Weigert stain for elastic tissue showed the persistence of small elastic

tissue fibers in several areas in the infiltrate, while in other places the elastic tissue fibers appeared to be swollen and broken

We thought it possible that this growth might be a hystiocytoma, or tumor of connective tissue origin. Dr. Satenstein, on the other hand, stated the belief that it was a Recklinghausen tumor. Here again there was a difference of opinion regarding the histologic section. The lesion had been present as long as the patient could remember, and although it was clinically mistaken for a "common mole," the histologic examination proved that it did not belong in this category

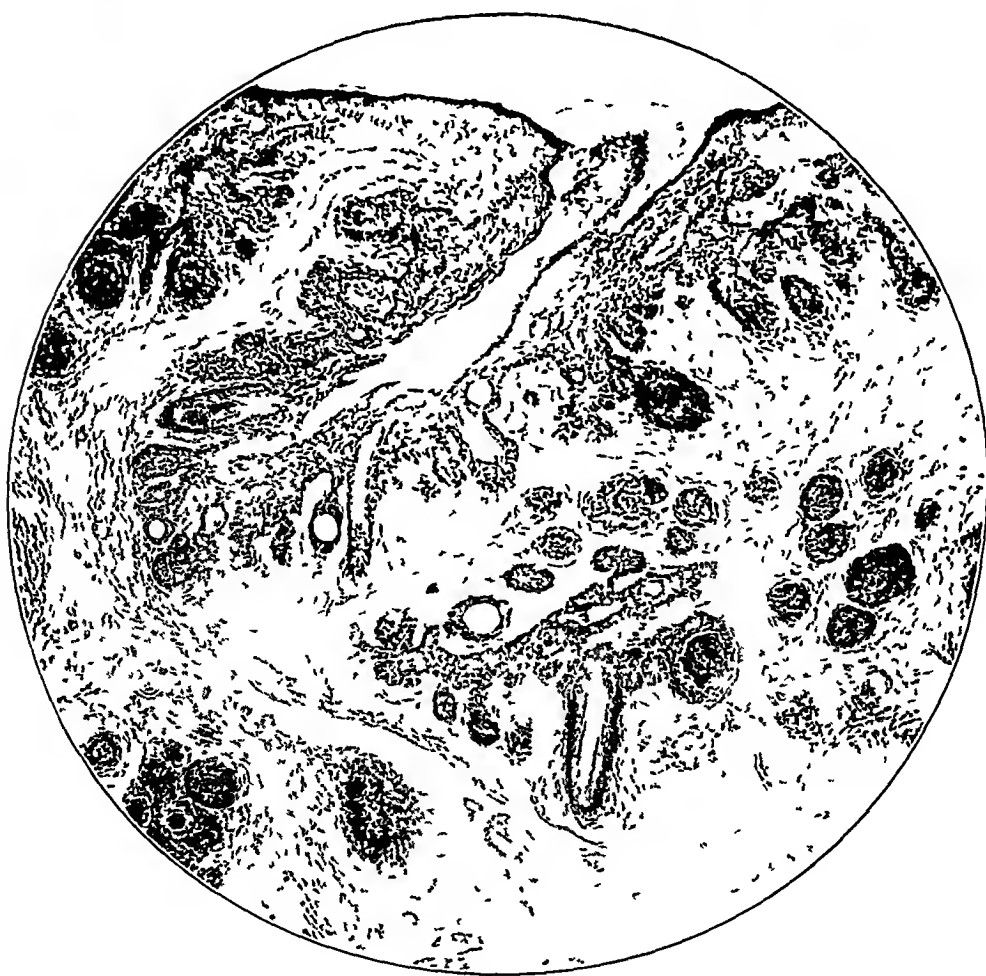


Fig 9 (case 7) —Tumor of connective tissue origin? Recklinghausen's tumor?

CASE 8—A M, a man aged 63, had two lesions on the forehead, which had been present for many years. Both appeared to be smooth and free of hairs. The one on the right side was pea sized, soft and light brown and had not grown, as it seemed to show the attributes of a "common mole," it was destroyed by desiccation. The other lesion was slightly larger, somewhat firm and fleshy pink and was situated near the scalp line to the left of the midline. The center showed many irregular depressions. There had been a slight increase in size in the past two years. The growth was removed and the base desiccated. A cross section showed that the tissue was relatively firm and that it had a dead white color.



Fig 10 (case 8)—Trichoepithelioma Mistaken clinically for a "common mole"



The diagnosis was trichoepithelioma, with its origin in the hair follicles. The central depressions were caused by dilatation of the follicular openings.

The nature of the first lesion destroyed, which had seemed to be an ordinary mole, must be reevaluated in the light of the microscopic observations of the second nodule. It appeared probable that growths of the nature of trichoepithelioma occurred more commonly than was suspected and that their incidence would be appreciably increased if tissue were regularly submitted for histologic study. It was possible that the cases of so-called basal cell epithelioma arising on the basis of a mole or pigmented nevus belonged in this category.

CASE 9—H. S., a woman aged 42, presented on her right temple what appeared to be an ordinary small pigmented mole, with fine hairs. It had been present for many years. The point of interest, however, was a split pea-sized smooth yellowish growth situated on the dorsum of the nose. The surface showed some fine telangiectases. The lesion had never bled and had undergone a gradual increase in size in the past year. The original growth at this site had been present for nine years, when in October 1933 it was removed by electrolysis. At that time it was regarded as of the same nature as the one on the right temple ("common mole"). After the removal, there was a gradual recurrence, more marked in the past year. In order to ascertain the nature of this recurrence, the lesion was excised in August 1937. At the end of two weeks the area had healed completely.

On histologic examination the epidermis was found to be approximately normal, with a few isolated hyperkeratotic accumulations in what appeared to be the openings of hair follicles or sebaceous glands. The growth was composed chiefly of large numbers of hypertrophied sebaceous glands. There were also numerous sweat glands. A moderate infiltration of round cells was observed about some of the blood vessels in the subpapillary layer, and the papillary zone revealed a few dilated capillaries. There were no nevus cells. The pathologic diagnosis was hypertrophied sebaceous glands, possibly a sebaceous adenoma.

From the nature of the microscopic anatomy, considerable doubt must be placed on the original diagnosis of mole in the sense in which that growth has been defined in this paper. The nature of the pathologic process probably explained the recurrence, for the major part of the growth was lodged deep in the cutis and its removal could not have been accomplished without some degree of scarring. In what seemed to be a case of recurrent mole, it was thought advisable to remove the growth in toto in order to establish the diagnosis and also to rule out any malignant change. This case illustrated another, perhaps not infrequent, possible clinical error in diagnosis of the common mole.

CASE 10—M. M., a girl aged 17, presented a smooth dark brown nonhairy elevated nodule, measuring 7 mm. by 1 cm., on the left side of the forehead about 2.5 cm. from the hair line. The duration was said to have been between four and six months. The lesion on the forehead had been traumatized by the patient, with a resultant increase in its size. A portion of the lesion on the forehead was removed for microscopic examination, and after the receipt of the pathologic report, complete excision was advised. In addition to the lesion on the forehead, the patient presented other smaller and flatter pigmented marks on the left cheek, chin and chest which were said to have been present since birth. None of these seemed to show any evidence of activity.

The histologic section showed an epidermis that was fairly normal, with pigment in the basal epidermis, free in the upper part of the cutis and in the neoplasm cells. There were no mitotic figures but there were many multinucleated cells. True clear cells were no longer present in abundance there being only a few in the basal zone. Cellular elements in the cutis proper were variously sized and

shaped, some round, some polygonal and some spindle shaped, they contained large vesicular nuclei, a number were multinucleated, some were very small and some were infiltrating between bundles of connective tissue. Scattered throughout the entire cutis were large hyperchromatic cells, some isolated and some in strands and whorls. In the papillary zone there was considerable disintegration of cell bodies in the majority of the cells. Pigment was present in the upper part of the corium and in the papillary bodies. There were a few telangiectases. Segmentation with the formation of *thèques* was profuse throughout the section.



Fig 12 (case 10)—Junction type nevus

This condition must be looked on as a proliferating and infiltrating stage of a nevus of the junction type.

CASE 11—M R, a girl aged 14, presented an area made up of many small roughly triangular and flat smooth pigmented nonhairy macules on the right lateral aspect of the chin, which had been present since birth. The area extended from the right side of the lower lip down to the upper part of the neck near the lower angle of the inferior maxilla. There was a pea-sized lesion, brownish in the center, with slight reddish tint at the periphery, at times it seemed more reddish, resembling an angioma, at other times it had a definite brown hue, as seen in an ordinary mole. The growth, which was smooth and slightly elevated, was removed for microscopic examination.

The section showed evidence of nevocarcinoma. Extending from the bottom of the section up to the epidermis was a dense epithelial cellular infiltrate. In the lower border of the epidermis there were groups and nests of cells similar to those in the cutis. The latter were not closely packed and had large hyperchromatic nuclei and definite bodies, and in places outlines of the cells could be seen which in some areas were multinucleated. In this area also there was a large amount of pigment. In the middle and deep portions of the cutis the cells were closely packed and took on spindle shapes.

The sections were submitted to Drs. Ewing and Fraser, who agreed that they showed no malignant change and that the condition was a neurofibroma with surrounding nevus, benign in character. Dr. Ewing expressed the opinion that the lesion should be treated with radium. Other sections were examined by Dr. S. W. Becker, of Chicago, who made the following report:

The section showed characteristics midway between those of a benign melanoma, or, in other words, a pigmented nevus, and a definitely malignant tumor. The deeper portions of the section gave no hint of malignant degeneration and were probably benign. The fact that pigmentation was limited to the superficial



Fig. 13 (case 11) —Junction type nevus? Pigmented patch of Recklinghausen's disease?

portion also was in favor of a benign condition. The groups of cells just beneath the epidermis situated in vacuole-like spaces were similar to those found in malignant neoplasms. They were not grouped together in masses, as in ordinary pigmented nevus, but were rather arranged at the periphery of the vacuole-like spaces, with the cellular process extending to the center and through the space. From the histologic picture, one surmised that the cells in the superficial portion were not entirely quiescent. Dr. Becker doubted, however, that a definite diagnosis of malignant melanoma could be made. He stated that, owing to the fact that the tumor was not a strictly quiescent nevus, it certainly would be advisable to treat it a "little more radically" than would be necessary for a quiescent lesion. Dr. Satenstein diagnosed the growth as a nevocarcinoma. Clinically, we felt this lesion was definitely benign, and in the two to three years that we have followed this patient, nothing has occurred to change this view.

CASE 12—H. B., a man aged 23, had a growth on the flexor surface of the left forearm which had originated about six years ago. The mark, which was roughly circular in outline, measured about 15 by 25 cm. Its surface was irregular, smooth and devoid of hairs. There was a narrow peripheral ring which was light brown, while the central portion was dark brown, with two relatively

firm elevated areas surrounded by a zone that was slightly less pigmented. The patient stated that there had been no increase in size during the past two or three years, but he believed that the central papules had fused somewhat during that period. The lesion was excised widely and closed with deimal sutures. There was a pea-sized smooth brown lesion on the upper part of the left arm, of unknown duration. This lesion was also removed. On microscopic examination the lesion of the forearm showed an epidermis with decidedly irregular rete pegs and pigment both in the epidermis and in the upper part of the corium. There were strands of hyperchromatic epidermal cells. The changes were typical of the junction type nevus. The second section taken from the arm showed an epidermis with



Fig 14 (case 13)—Junction type nevus before removal

irregular projections and infiltrating nevus cells in the corium and a slight amount of pigment. The diagnosis was intradermal nevus.

CASE 13—S M, a man aged 19, stated that the growth on the dorsum of the right foot had not appeared until two months before the present observation. The lesion measured 8 by 12 cm and was smooth, slightly elevated, uniformly deep, brownish black and devoid of hairs. It had appeared suddenly. There was no history of trauma to that area or of a previous spot at the site. By means of the cutting current, the lesion was removed widely (fig 14) with a 2 cm border of normal skin. The wound healed completely without skin grafting.

Microscopic examination (fig 15) of many sections showed that the entire growth had been removed and that a great deal of apparently normal tissue had

been included. The lesion appeared to be well localized chiefly in the lower epidermis and the immediately adjacent cutis. A large amount of pigment was observed in these areas as well as some in the upper portion of the epidermis, including the corneous layer. The major portion of the growth was composed of groups of cells (segregation) within *thèques* in the lower part of the epidermis. The cells showed nuclei of various shapes, with large conspicuous nucleoli and well developed particles of chromatin. The protoplasmic outlines were difficult to

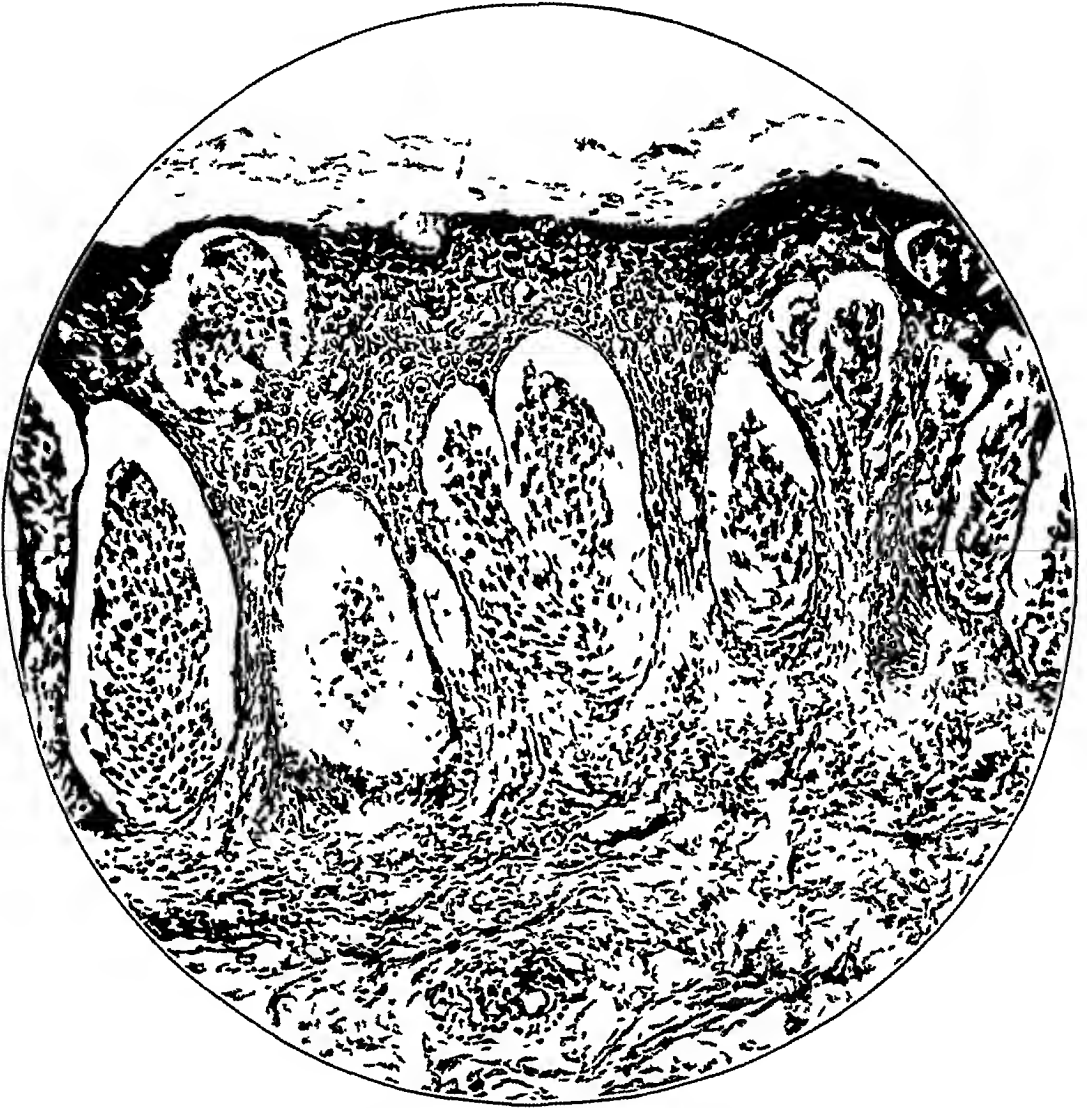


Fig 15 (case 13) —Junction type nevus

distinguish owing to the paleness of the cytoplasm. There were some large cells containing two nuclei and cytoplasm staining a deeper pink. Many cells showed pigment, usually in the form of fine granules and sometimes in larger granules, but on the whole these deposits were fairly uniform in size. Similar groups of cells were found just beneath the corneous layer, giving the impression that they were just about to be cast off. In the papillary and subpapillary layers were larger cells of various sizes which contained rather large granules of pigment of fairly uniform size and obscured the outlines of the protoplasm. However, it

appeared that the cells were disposed in sheets. In the nearby surrounding tissue in the corium, there was an inflammatory reaction in the form of several blood vessels surrounded by lymphocytes and a few plasma cells. There were no mitotic figures. The pigment was bleached by means of potassium permanganate and oxalic acid.

The diagnosis was junction nevus. The segregation with the development of *thèques*, which was one of the principal changes in this case, taken together with the other observations already enumerated, makes this type appear to be a rather dangerous lesion. Clinically, but for its unfavorable location and its smooth character devoid of hairs it did not look like a malignant growth.

CASE 14—H. B., a woman aged 33, had an irregularly shaped dark brownish black slightly elevated mark, the surface of which was uneven but not warty, just anterior to the right ear and at the lower border of the hair margin. The color of the lesion was uneven, being brownish with some darker black portions. The mark measured $\frac{1}{2}$ by $\frac{3}{4}$ inches (13 by 19 cm). There were numerous coarse black hairs, but it was difficult to determine whether they were peculiar to the nevus or whether the mark simply happened to be in a location where hair was normally present. There was a tiny ulceration in the center of the lesion that had bled. The patient was uncertain as to the exact duration but was certain that it had grown considerably in the past year or two. The lesion was excised, and the microscopic examination proved it to be a typical nevus of the junction type.

CASE 15—A. M., a woman aged 22, was born with a nevus on her right cheek near the angle of the jaw. It was an irregularly lobulated oval brownish lesion about 2 cm in its longest diameter. The central portion was light brown, while a narrow periphery was darker brown. In the center, also, there was a small irregular fleshy brown raised area. The growth revealed many stiff hairs, some of these had been clipped by the patient, but none had been plucked. There had apparently been no increase in size from birth, nor had the lesion ever bled as a result of trauma. With the aid of local anesthesia the lesion was excised, complete healing occurred within a month.

Microscopic study showed the raised portion of the lesion to be composed of nevus cells in typical configurations, accompanied by thinning of the epidermis in the usual fashion. At the periphery of the section the epidermal layers showed a moderate degree of proliferation, which was considered normal by Dr. E. A. Barthel and evidence of the junction type change by Dr. Satenstein. Many hair follicles were observed throughout the section. The flat portion of the lesion showed essentially the same alterations except that the epithelial proliferation seemed to be composed chiefly of what might be called clear cells. The diagnosis was intradermal nevus in combination with the junction type.

CASE 16—A. M., a woman aged 45, presented a growth on the right side of her back which she stated was of six months' duration. The back and shoulders were covered with many freckle-sized pigmentary macules. The growth in question appeared to arise from the upper pole of a relatively flat smooth light brown pigmented area about 1 cm in diameter. It was a shiny smooth black mass measuring 1.5 by 0.5 cm. There were no hairs. It had increased rather rapidly in size, and the patient mentioned that she thought it had developed from a freckle (*lentigo maligna*).



Fig. 16 (case 14). Junction type nevus.



Fig. 17 (case 14). Low power section of junction type nevus



Fig 18 (case 15) —Intradermal nevus in combination with junction type nevus.

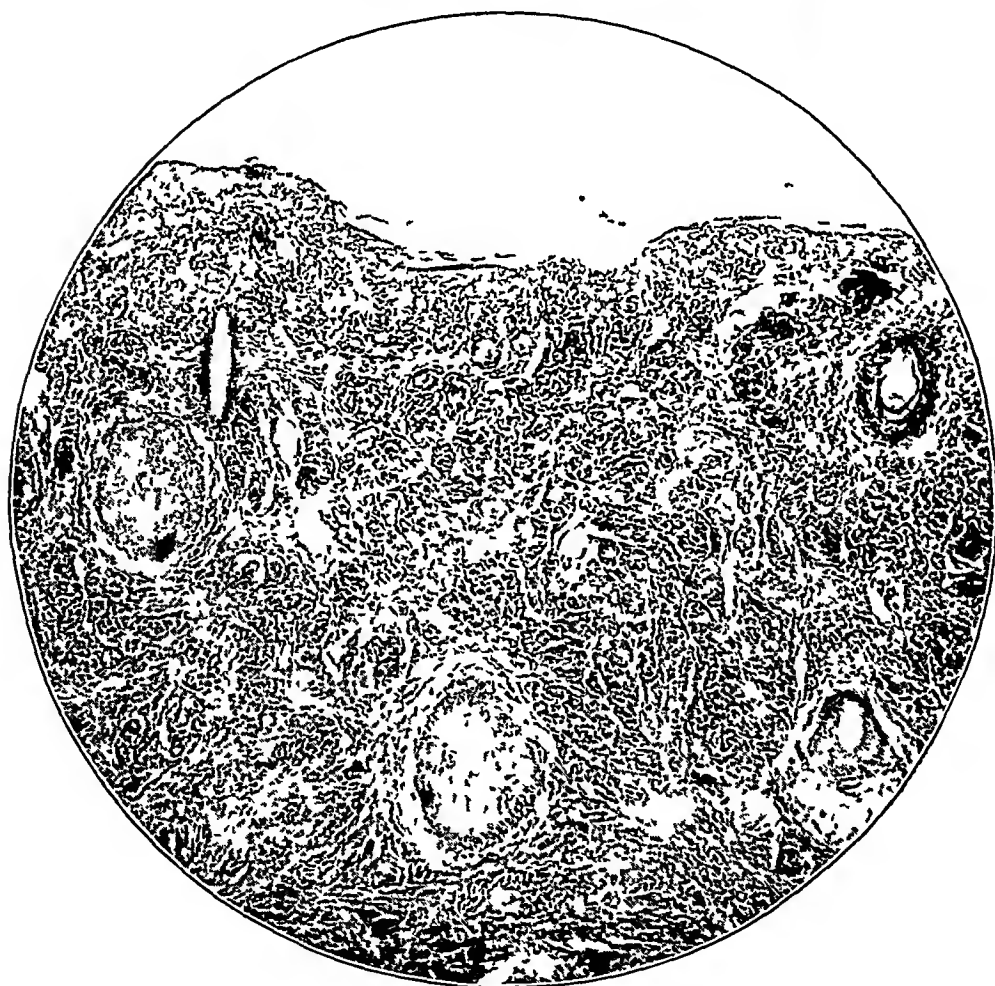


Fig 19 (case 15) —Low power section of intradermal nevus in combination with junction type nevus

Microscopic examination showed that the epidermis was thinned and flattened. A large mass lined at the sides by epidermis dipped down as far as the middle part of the cutis and enclosed a group of cells of various size, some containing two or more nuclei. The cells had distinct bodies, and some also had distinct outlines. Some of the nuclei were large, and there was a fair number of mitotic figures. The vessels around the mass were considerably dilated, and around them there was a moderate amount of focal cellular infiltration. Moreover, there was an intense diffuse cell infiltration, with many small thin-walled vessels. It consisted mainly of small round cells, a few plasma cells and connective tissue cells, some with pigment. The mass in areas reached within the basal zone of the epidermis. The diagnosis was a nevus of the typical junction type.

CASE 17—H. A., a woman aged 42, had a smooth pea-sized slate blue lesion on the dorsum of the left hand, which had been present at birth or had appeared shortly after. The color was uneven, the peripheral blue was darker than that

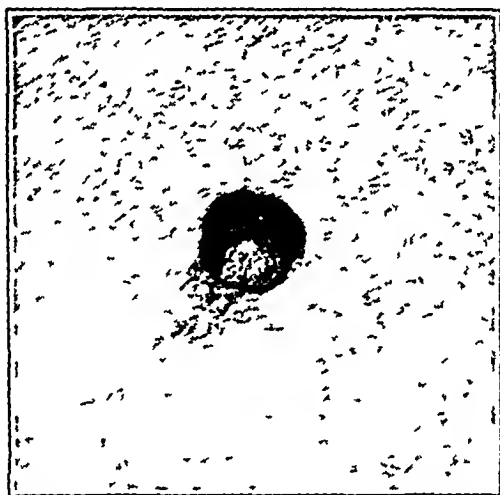


Fig. 20 (case 16)—Junction type nevus

in the center. There had been no bleeding and no increase in size. The growth was removed by wide excision.

Histologic examination (fig. 22) showed an epidermis that was apparently unchanged. There were many cells of the *cellule claire* type in the basal layer. In the middle two thirds of the cutis there were numerous stellate cells containing pigment in the form of coarse granules that seemed to be nearly uniform in size and shape. In this area of pigmentation the collagen bundles seemed undisturbed except that there was a proliferation of spindle-shaped fibroblastic nuclei. In this zone also the pigment was distributed especially densely about the sweat glands, possibly in relation to the blood supply about these structures. The distribution about the vessels was also noted in the papillary bodies, where, however, there was much less pigment and that present appeared to be restricted to the parts directly adjacent to the capillary walls. There were some deposits of pigment that seemed to lie freely in the interstitial tissues, but this impression was probably caused by cross sections through the cytoplasm of the connective tissue cells. The distribution of the pigment appeared to explain the lack of uniformity in the color of the lesion, creating what has been called a speckled appearance. The diagnosis was blue nevus.

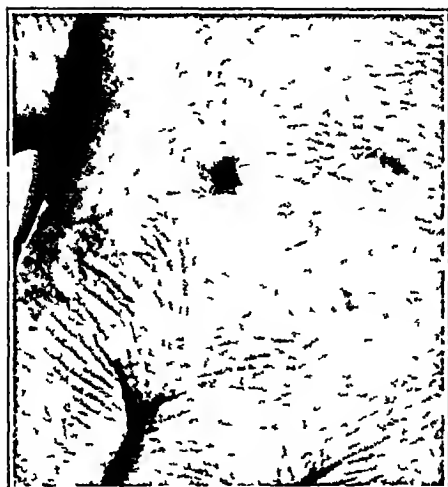


Fig 21 (case 17) —Blue nevus

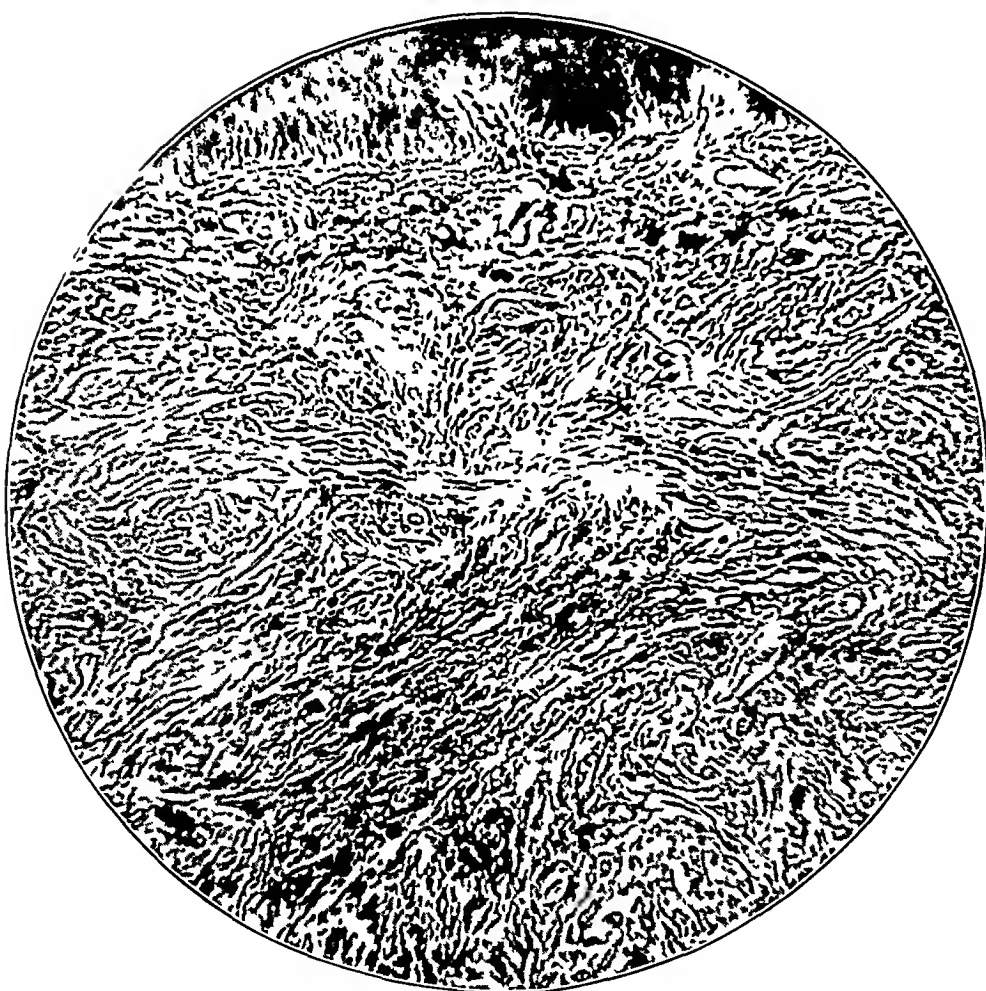


Fig 22 (case 17) —Blue nevus

From birth, also, there had been present a pea-sized relatively smooth moderately firm skin-colored lesion on the right cheek near the nose, the growth showed a definite brownish tone, particularly in the center, with a few telangiectatic vessels. There were some delicate hairs. There had been no bleeding or evident increase in size. The entire growth, together with the surrounding normal skin, was excised and on histologic examination proved to be a typical intra-dermal nevus.

SUMMARY AND CONCLUSIONS

The need to establish a simplified uniform nomenclature, so that each term used has a specific, universally recognized meaning, is of paramount importance. An outline is submitted to assist in the classification of pigmented nevi and moles from both the clinical and the histologic standpoint.

The relation of the various marks to cancer is clearly defined, and illustrative case records and photographs are included.

Reasons are given for restricting the designation "common mole" to that type of lesion characterized histologically by intradermal collections of nevus cells. We find no evidence that the "common mole" (the pure form, not combination types) ever develops into cancer.

Malignant melanomas apparently have their origin in nevi of the junction type, which are clinically characterized as smooth nonhairy pigmented spots.

The blue nevus appears to be a benign lesion and should not be confused with the dangerous slate black or blue-black melanoma.

ABSTRACT OF DISCUSSION

DR FRED WISE, New York. I once had occasion to treat a brown hairy mole in the clinic while Dr Bruno Bloch stood by. As I was about to apply the solid carbon dioxide pencil, Dr Bloch grabbed my arm and said, "Don't do that!" I said, "Why not?" He replied, "Because you are liable to cause a malignant growth." To my question whether he had ever encountered malignant changes subsequent to the treatment of brown hairy moles, he replied that he had seen several of them. In my own experience no such thing has occurred. You will recall the photograph on the screen, demonstrated by Dr Traub, of a pale, flat, pigmented nevus on the left side of the chin of a young girl. She was originally under my observation at the clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. I advised treatment with solid carbon dioxide, because I could determine by clinical observation that the mole was a simple pigmented nevus of the smooth and pale variety. Subsequent events proved this to be the correct diagnosis. A small section of the mole was examined microscopically, the histologic description, however, included the term "malignancy," much to my astonishment. In many instances of this type the clinical diagnosis seems to have more weight than the microscopic, Dr Traub's case is a good example.

DR RUBEN NOMLAND, Chicago. How does Dr Traub explain the so-called implantation melanoma of the sole? I have observed several cases in which a dark spot developed on the sole after prolonged irritation (usually by a nail in

the shoe) and then after a variable period, five to twenty years, a malignant melanoma developed. What is the explanation of such a finding?

I should also like to question Dr Traub concerning the treatment of such lesions and to ask him how he explains the development in senile persons of pigmented lesions with extremely dark pigment, which occasionally undergo malignant change.

DR J GARDNER HOPKINS, New York. When I answered Dr Traub's questionnaire I had to say that I have never observed the development of malignant change in a mole which I had previously observed in an apparently benign stage. However, physicians must all have seen malignant melanomas which the patient stated had originated from an ordinary mole.

Dr Traub brings up the fundamental question whether supposed moles which develop into lethal metastasizing tumors are identical with the innumerable moles which remain harmless or whether they have special malignant potentialities from the beginning. I wish he would explain further how he differentiates the two groups, either in clinical or in histologic terms.

DR GEORGE M. MACKEF, New York. Dr Traub's paper is really a preliminary report. He is endeavoring to find a way to determine on clinical grounds the danger associated with the different varieties of nevi. He has made some headway, but he has an enormous amount of work ahead of him. What dermatologists are trying to do is to classify moles and nevi clinically, largely for the sake of convenience, study the clinical appearance and behavior, agree on the clinical diagnosis and then verify or refute the clinical diagnosis histologically. It has been interesting work. Often, indeed, the clinical diagnosis is erroneous, but as a result of this experience one is clinically correct more often than formerly. One hears the terms common mole and blue-black mole, also, there is a difference of opinion as to the potential danger inherent in the different moles. It is hoped that eventually it will be possible to classify moles clinically, give them convenient names, estimate the degree of potential danger and outline therapy in relation to these facts. One realizes, of course, that histologically there is no precancerosis, but certainly some moles are more likely to become malignant than are others. It is important to be able to differentiate clinically between benign and malignant moles and to estimate the potentialities of benign moles. Dr Traub has had some success. I hope that he will continue with this difficult task and have further success.

DR NELSON P. ANDERSON, Los Angeles. Physicians are all familiar with the ordinary brown pigmentation that occurs in the vicinity of some melanomas that are actually malignant. I believe that so-called brown moles which have become malignant are moles which have originated from a minute group of nevus cells and that the characteristic brown pigmentation about them is that of a nevus or melanoma which has already undergone malignant change. This possibly explains in some instances the patient's statement that he had a simple brown mole in the affected area.

DR FRED D. WEIDMAN, Philadelphia. If there is any one kind of lesion that comes with greater frequency than another through a laboratory, it is the mole, and opinion ought to be well crystallized by now, yet it is not. I should like particularly to get further information from Dr Traub as to the differentiation the authors make between the true blue nevus and the other blue mole of the epidermis, which may be their "junction lesion" as I understand it. According to Jadassohn, the blueness depends on the depth of the pigment, this seems to be generally accepted, but I do not know that it is absolutely proved. In any event,

the pigment in an epidermal nevus may lie just as deep as the pigment in a blue nevus, and the lesion could be rated clinically as blue-black nevus. Incidentally, at a recent conference the registry committee of this association disagreed as to the likelihood of malignant change developing in the blue nevus. Dr. Satenstein said that he had never seen it.

One should not attempt to classify a congenital lesion, such as a nevus, as malignant or nonmalignant on purely statistical grounds, that is, on the basis of its location in the epidermis, at the junction point or in the corium. I think that can be done only after the accumulation of ample statistics and after analysis and resolution of the data. I doubt that any such analysis has been made. Until it has been made, I feel that it is necessary to decide whether a lesion is malignant or not on histologic criteria which general pathologists have known for years. In the final analysis there are two such criteria. The first is evidence of some cellular change indicating an alteration in the direction of malignancy. McCarthy's "one-eyed cells" are in point here; they have been described in contributions from the Mayo Clinic, where pathologists feel that they can identify an individual cell as genuinely cancerous. Only the trained pathologist is qualified to attempt this.

The second criterion of malignancy is permeation and invasion of tissue. If it can be determined that certain nevus cells are extending beyond the usual realm of ordinary nevus cells, say into the level of the sweat glands, the process is malignant. Until there are ample, complete and convincing statistics on data such as those reported today, physicians should depend on these two items. One must remember that the nevus does not follow accurately the rules for normal epithelium, because it is a congenital anomaly. That being the case, the epithelium must be expected to be found in positions deep in the lymphatic spaces, positions which the general pathologist will say are abnormal for epithelial cells, ergo, cancer. Consequently, the general pathologist commonly and erroneously diagnoses benign nevi as cancerous. It is only after the general pathologist has had some experience along these lines that he learns his lesson. Fortunately, the American Association of Pathologists and Bacteriologists has selected the pathology of the skin as its main theme for discussion this year. Dr. Lee McCarthy is the dermatologic consultant, and general pathologists will be advised in this most important matter.

DR EUGENE F. TRAUB, New York. In the case of the flat, smooth, pigmented, nonhairy nevus on the young girl's chin, we simply removed a specimen to add to our collection, never for a moment believing that there might be a question of malignancy. Nevertheless, two New York pathologists independently called the lesion a malignant melanoma, while a third thought it might be one of the pigment spots of von Recklinghausen's disease. Dr. Becker of Chicago also had an opportunity to study this slide, and he was doubtful as to whether the process was benign or malignant. A great difference of opinion, therefore, is possible after examination of sections from such lesions, just as it is when the patient is studied solely from a clinical standpoint. The classification just submitted unquestionably is far from perfect and must be subject to revision and correction, but it seems to me that even an imperfect classification which can be revised as additional information is forthcoming is better than none. It may at least help to simplify the terminology, a distinct advance in itself.

There is considerable difference of opinion as to the actual importance of trauma, especially with some of these growths, and there are other factors, naturally, as Dr. Weidman pointed out, which help to determine whether or not the lesion is going to be cancerous. I feel that many lesions which are assumed to have originated from nevi are malignant from the onset and have had no

relation to any type of nevus, even though some sort of mark may have been present for many years. I refer particularly to the type of mark that might have been assumed to be a nevus rather than a "senile freckle" or premalignant spot of the sort seen in aged persons. It is an accepted fact that not all malignant melanomas originate from nevi. While the majority of authors state that a rather high percentage of malignant melanomas do so originate, it is probable that more careful investigation of histories and further study may prove the estimate rather high. That is another reason why one should be careful about terminology in describing the original mark, so that future authors collecting such statistics will not confuse the issue. It is often a mistake to accept a patient's unsupported account of the presence or absence of a preexisting mole on which malignancy has developed.

To answer the question about implantation of melanomas, I refer you to the recent work by Peer and Paddock. While this question is still in dispute and cannot be finally settled at this time, Peer and Paddock, who buried full thickness skin grafts and other skin grafts from which the epidermis had been shaved off and subsequently removed these areas for microscopic study, showed what might be expected to happen to implanted particles of skin. They found that in a comparatively short time all portions of the epidermis and the cutis, even including the hair follicles and hairs (but with the exception of the sweat glands in some instances), were absorbed and had disappeared. Therefore, probably any epidermal structure that might be carried in by an instrument or nail puncture is absorbed before it can start a new growth. Of course, a puncture wound may, without carrying cells down into the deeper tissues, give rise to a melanoma in some other way, perhaps by direct injury to some of the pigment-forming cells themselves.

Concerning Dr. Weidman's question about the blue nevus, one must again admit to a difference of opinion. Satenstein, Becker and others who have had a wide experience in examining such sections have never seen a malignant growth result from such a lesion. In our series we have not seen a blue nevus become malignant. It is possible that in cases in which a malignant melanoma developed the original lesion was not a blue nevus but some other pigmented mark clinically resembling it. There are a number of marks which clinically resemble the blue nevus, so that in some instances a histologic examination is necessary before the diagnosis can be definitely established. In cases in which malignant change has been described as developing in a blue nevus, the growth has been a melanosarcoma. No doubt some of the slate black moles which are junction nevi and potentially malignant melanomas and which differ widely histologically from the blue nevus are the lesions that cause the confusion.

The type of lesion that I believe to be innocent is the hairy pigmented nevus. When hair is an essential part of the nevus, regardless of the color, in most instances the lesion remains benign. The warty lesions are also, in our opinion, unlikely forerunners of malignant melanoma. It is the smooth, flat, pigmented, nonhairy and nonwarty lesion that is most dangerous. The color apparently is not of great importance.

LXXXIII—MALASSEZIA FURFUR, THE CAUSE OF TINEA VERSICOLOR

CULTIVATION OF THE ORGANISM AND EXPERIMENTAL PRODUCTION OF THE DISEASE

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University School of Medicine

ST LOUIS

The cultivation of *Malassezia furfur*, the fungus responsible for the disease pityriasis (tinea) versicolor, has been seldom accomplished, in spite of the large number of cells of the organism in the stratum corneum of the epidermis. After making several unsuccessful attempts, I finally cultured it and reported my work in a previous paper¹

It is the purpose of this communication to review briefly the characteristics of the organism in tissue and in culture and to give further data as to the experimental inoculation of the fungus into laboratory animals, human volunteers and the chorioallantoic membrane of the developing chick

HISTORICAL REVIEW

Tinea versicolor was first recognized and demonstrated as a fungous infection by Eichstedt². In 1864 Kobner³ claimed to have transferred the fungus to his own skin and to that of rabbits. Hallier⁴ observed the growth of an organism which he first classified as an *Aspergillus* and then as a *Stemphylium*. Neumann⁵ observed the formation of

Studies, observations and reports from the Laboratory for Mycology and Dermatological Research of the Barnard Free Skin and Cancer Hospital, service of Dr M F Engman Sr

1 Moore, M. Cultivation of *Malassezia Furfur*, Etiological Agent of Pityriasis (Tinea) Versicolor, *Mycopathologia* 1 53, 1938

2 Eichstedt, E. Ueber die Kratzmilben des Menschen, ihre Entwicklung und ihr Verhältniss zur Kratze, *Notiz a d Geb d Natur- u Heilk* 38 105, 1846

3 Kobner, H. Klinische und experimentelle Mittheilungen aus der Dermatologie und Syphilidologie, Erlangen, F Enke, 1864, p 41

4 Hallier, C. Die pflanzlichen Parasiten des menschlichen Körpers, Leipzig, Wilhelm Engelmann, 1866, p 79

5 Neumann, I. Textbook of Skin Diseases, translated from the second German edition by A Pullar, London R Hardwicke, 1871, p 322

daughter cells of the fungus into tubular structures but did not isolate the microbe. Von Sehlen⁶ and Unna cultured an organism which was septate and branched at the ends, liquefied gelatin and became brown in culture. Kotljarsky⁷ isolated a fungus from scales with which he produced brown spots on a dog. His microbe was named *Oidium subtile*, but it appeared to be a possible species of *Actinomyces*. Spietschka⁸ used sterilized urine in his mediums and obtained a slowly growing fungus in 12 instances. He inoculated 6 human volunteers and himself, with negative results in all but a 22 year old patient with lupus who showed browning after nine days.

Matzenauer⁹ used various sugar mediums and was able to isolate two colonies on Fingert's "epidermin agar" from several hundred poured plates. To this author should be given the credit for having successfully cultivated *M. furfur*. He inoculated himself with this fungus and noted a lesion three months later. Gastou and Nicolau¹⁰ confirmed Matzenauer's work, using placental extract in their medium. They cultured the organism on three occasions.

Little work had been done since these reports until 1923, when Schmitter¹¹ isolated an organism which suggested a bacterial contamination. Nine years later Kambayashi¹² reported the growth of a fungus nine months after inoculation. The length of time necessary for the development of the microbe and its growth near the rim of the plate suggested a contamination. In 1937 Marquardt¹³ used Grütz's medium¹⁴ and obtained growth in five of eleven attempts. His inoculations in guinea pigs and human beings gave negative results.

6 von Sehlen. Ueber die Zuchtung von *Pityriasis versicolor*, *Tagebl d Versamml deutsch Naturf u Aerzte*, 1880, p 600

7 Kotljarsky, E J. *Morphologie des Mikrosporon furfur*, *Vratch*, 1892, no 42, p 1055, no 43, p 1083, abstracted, *Arch f Dermat u Syph* 26 312, 1894

8 Spietschka, T. *Untersuchungen uber das Mikrosporon furfur*, *Arch f Dermat u Syph* 37 65, 1896

9 Matzenauer, R. *Zur Bacteriologie der Pityriasis versicolor*, *Arch f Dermat u Syph* 56 163, 1901

10 Gastou and Nicolau. *Culture du microsporon furfur sur milieu solide placentaire*, *Bull Soc franç de dermat et syph* 13 222, 1902

11 Schmitter, F. *The Aetiological Fungi of Tinea Versicolor and Tinea Flava*, *J Trop Med* 26 190, 1923

12 Kambayashi, T. *Eine botanische Untersuchung des Mikrosporon furfur*, *Robin, Botan Mag, Tokyo* 46 232, 1932

13 Marquardt, F. *Die Kultur des Mikrosporon furfur*, *Dermat Wchnschr* 104 177, 1937

14 This medium consists of 9 Gm of agar, 25 Gm of peptone, 25 Gm of sodium chloride, 25 cc of glycerin and 30 Gm of "nervina malt" in 500 cc of distilled water

EXPERIMENTAL CULTURING

The cultivation of *Malassezia furfur* was successful in a broth medium (peptone, 1 per cent, and maltose, 4 per cent) after several years of attempts with various routine laboratory agar mediums

The lesions were cleansed with 70 per cent alcohol, scrapings were made with a sterile scalpel, and the cleansed scales were transplanted directly into tubes of the broth. *M. furfur* was grown on two occasions from the scales of 9 patients chosen at random when the cultures were incubated at 37 C. There was no growth in the tubes exposed to room temperature. The scales for both cultures were obtained from early, actively spreading lesions.

The cultures grew as small islets on the surface of the broth and as a sediment at the base of the tube. Subcultures from both growths and from the shaken-up growths always resulted in similar cultures.

DESCRIPTION OF THE FUNGUS

In young lesions *M. furfur* appears as a fine filamentous, branching mycelium, 1.5 to 2 microns in diameter (fig 1, 1). As the lesions become older, the fungus forms cross walls and short hyphal cells, 1.5 to 4 microns in diameter and 10 to 16 microns the length of the axis. These cells in turn become spherical free aithrosporous cells, vary from 3 to 8 microns in diameter, and are observed associated with the filaments in old lesions (fig 1, 2).

On artificial mediums when first grown the organism manifests itself as spherical budding cells at the base of the tube and as germinating fusiform-like cells at the surface. The latter cells produce cross walls, become elongated and branch. In subcultures of the growths colonies develop on various mediums which are flat and dull or moist, mucoid and shiny, verrucous, cerebriform to rugose, vermiculate and somewhat velvety, on moist agar in particular there develops an arborescent growth (fig 2). The color of the cultures varies in different mediums from whitish gray and fawn to creamy buff and light cinnamon in young cultures to ochraceous buff and dark cinnamon in older cultures. The colors seem to correspond to those observed in the lesions of human beings. As the growths of the fungus become old the organism loses its pigment.

Microscopically, the fungus in culture shows a characteristic development, which begins with the formation of a somewhat fusiform cell approximately 3 by 16 microns with convolutions and budlike projections at each end. As the cells increase in size they form a cross wall, become elongated, eventually produce more transverse septums and then branch. The hyphae measure approximately 1.5 to 5 microns in diameter. The filaments become beaded to form oidoid structures,

which are walled off and arthrospore-like and then spherical, ellipsoid or ovoid and thick walled, simulating the blastospores seen in scales of the infection. These cells measure approximately 4 to 10 microns in diameter, depending on the medium on which they are grown.



Fig 1—*Malassezia furfur* in lesions (1) biopsy section (low power) showing young filaments (methylene blue and eosin) and (2) histologic section showing spherical cells and filaments in older lesion (methylene blue and eosin, with oil immersion)

The fungus also produces chains of thick-walled, sclerotic cells, with fine nonseptate, dendritic and intertwining hyphae. Asci and ascospores

have not been observed in either old or young colonies or on favorable or unfavorable mediums

On biochemical study *M. furfur* liquefied gelatin beginning on the fifth day at the surface. Litmus milk was acidified after ten days but showed no curdling. Acid was produced, but no gas, with dextrose, d-oxylose, amygdalin and d-levulose. Neither acid nor gas was produced with maltose, rhamnose, raffinose, dextrin, d-mannitol, l-arabinose and starch.

EXPERIMENTAL INOCULATIONS

The ultimate proof of the etiologic significance of a fungus naturally rests with its ability to reproduce the disease for which it is held responsible. The inoculation of rabbits, guinea pigs, rats and mice gave negative results, both by the percutaneous method and by the direct

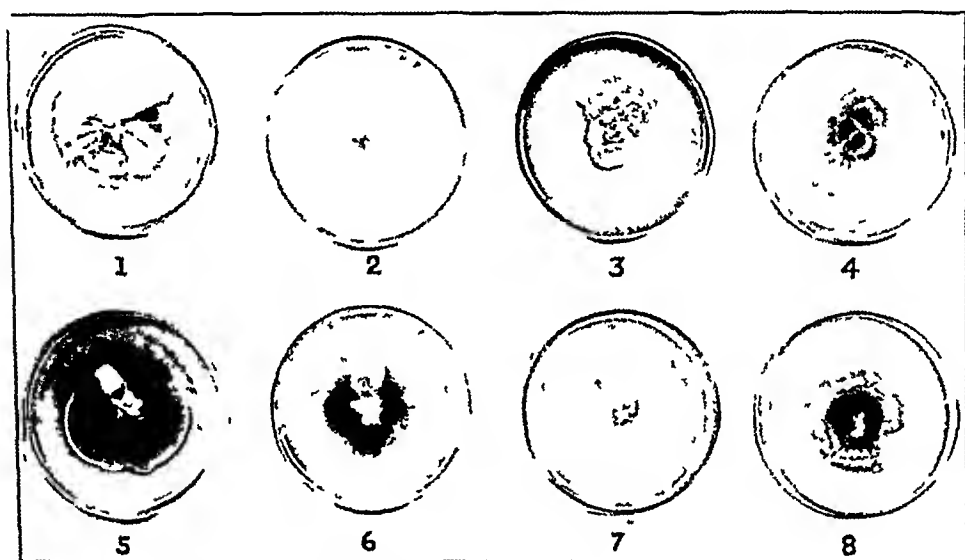


Fig 2—Agar cultures of *Malassezia furfur* (1) Czapek's, (2) corn meal, (3) wort, (4) Sabouraud's maltose, (5) Sabouraud's dextrose, (6) potato-dextrose, (7) nutrient and (8) glycerin

application of fungi to the intact skin. In rabbits and guinea pigs inoculated intracutaneously or intratesticularly granulomatous lesions developed which were hard, heavily infiltrated and erythematous and showed microscopically a heavy eosinophilic infiltrate.

Inoculations of the human skin (percutaneously or intact) gave favorable results in 3 of 8 volunteers. The reaction at the site of inoculation in 2 of the volunteers appeared as a follicular outgrowth, while a typical lesion starting in approximately two weeks, developed in the third person. Scrapings made from the site of inoculation in the third patient revealed the formation of spherical cells after the first week, with a complete conversion of the filaments into spherical cells after the third week. Scrapings made at weekly intervals revealed only

spherical cells for three weeks (fig 3, 1), but after the fourth week no formation was apparent as a result of the germination of the cells. Examination of scrapings from the site of inoculation in the fifth week revealed spherical cells and formation of filaments (fig 3, 2). When



Fig 3—*Malassezia furfur* in experimental lesion (1) spherical budding cells after three weeks (methylene blue and eosin, with oil immersion) and (2) spherical and germinating cells after five weeks (methylene blue and eosin, with oil immersion)

compared with the organism seen in scrapings from a spontaneous infection, the fungus observed in the experimental lesion after the fifth week presented similar morphologic structure and cellular measurements. *M. furfur* thus showed a reversion to its original parasitic state. The fungus grew profusely at the site of inoculation.

As a further method of determining the etiologic significance of the fungus isolated from lesions of pityriasis versicolor and identified as *M. furfur*, the microbe was transplanted directly onto the chorioallantoic membrane of the developing chick. The membranal reaction consisted

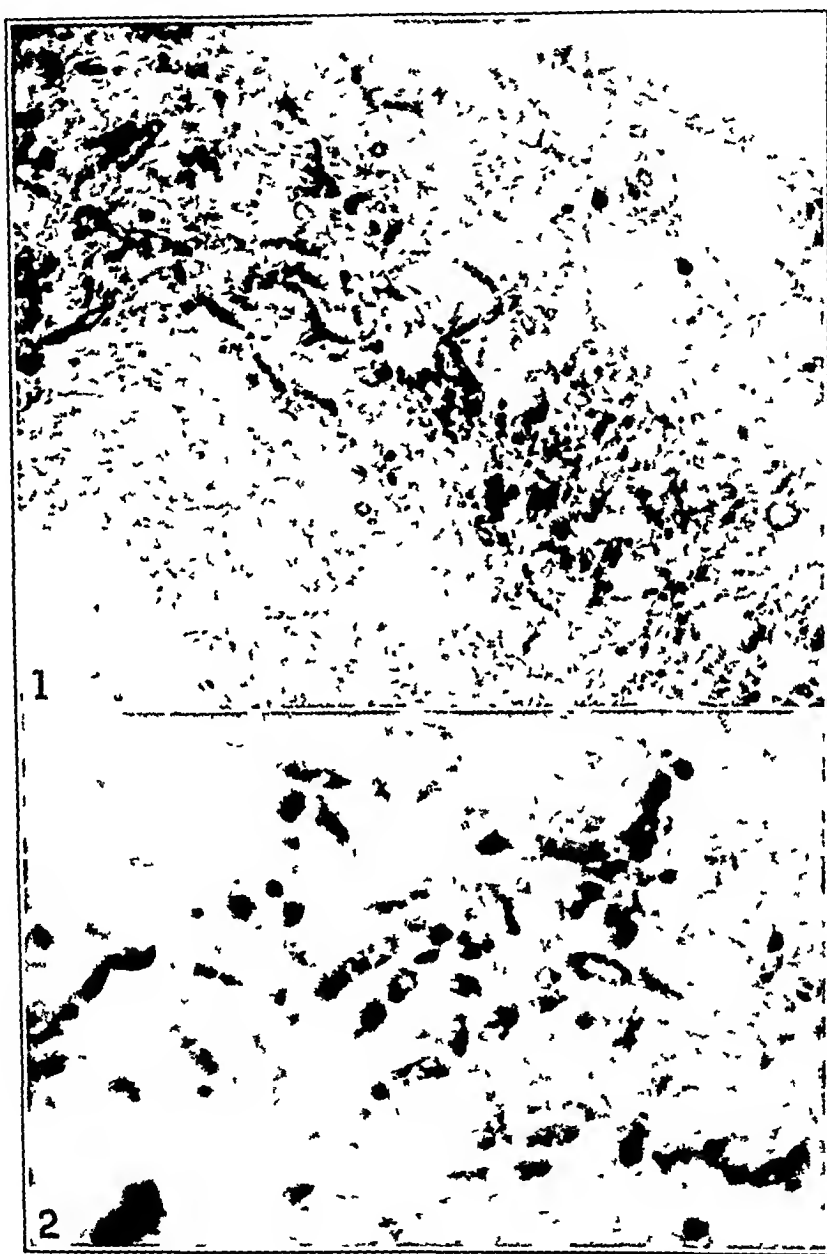


Fig 4—Photomicrographs of *malassezia furfur* (1) in peripheral growth of inoculum on chorioallantoic membrane of developing chick (450 \times) and (2) on chorioallantoic membrane (877 \times)

in a nodular growth which microscopically showed a heavy infiltrate of monocytes at the junction of the fungus inoculum and the ectoderm. The ectoderm was stimulated to marked proliferation of ectodermal cells, which invaded the mesoderm. The mesodermal layer showed, in addition to islets of ectodermal cells, groups of leukocytes, fibroblasts and

apparently ectodermal pearl formation, an indication of hyperkeratinization. Of chief interest, however, was the well developed growth of *M. furfur* at the periphery of the inoculum, with the appearance of the characteristic spherical cells and filaments seen in scrapings from a human lesion (fig 4).

SUMMARY

It is the purpose of this paper to emphasize again that *Malassezia furfur*, the cause of tinea versicolor, can be cultivated, as was first pointed out by Matzenauer in 1901, confirmed by Gastou and Nicolau in 1902 and further confirmed by me in 1938.

The presence of many different, harmless and cultivable fungi on the skin has complicated the true significance of the organism isolated by Matzenauer. The lack of conclusive evidence as to the pathogenicity of the numerous fungi isolated since Matzenauer's work and the adverse conditions of growth certainly help to rule out many of these organisms.

The fungus which is briefly described here was isolated on two occasions from 9 patients. It corresponds to the microbe described by Matzenauer and reproduces in culture the characteristics of *M. furfur* seen in scrapings from a spontaneous lesion. The organism in culture, however, shows varying cellular measurements which is due to the constituents of the medium on which it is grown. The cultures vary widely in appearance, depending on the medium employed.

The fungus liquefied gelatin beginning on the fifth day. Litmus milk was acidified after ten days, without curdling. Acid was produced, but no gas, with dextrose, d-xylose, amygdalin and d-levulose. There was no acid or gas produced with maltose, lactose, saccharose, d-galactose, rhamnose, raffinose, dextrin, d-mannitol, l-arabinose or starch.

Experimental inoculations by the percutaneous method or by the application of the fungus to the intact skin of rabbits, guinea pigs, rats and mice gave negative results. Intracutaneous and intratesticular inoculations in rabbits and guinea pigs resulted in granulomatous lesions which were infiltrated, erythematous and hard. The inoculation of human volunteers either percutaneously or by the application of fungi to the intact skin gave favorable results in 3 of 8 volunteers. In 2 follicular outgrowths developed at the site of inoculation, while in 1 a typical lesion developed, starting in approximately two weeks. The organism grew profusely at the site of inoculation, first as a spherical budding cell for approximately three weeks, then, as a result of the germination of these cells, filaments and blastospore-like cells developed to simulate the microbe in its parasitic role. As a further check, the fungus was transplanted onto the chorioallantoic membrane of the developing chick, where it produced a reaction in the layers of this structure, with a reversion of the cells to the morphologic structure characteristically seen in scrapings from lesions of human beings.

LXXXVIII—A SEARCH FOR FILTRABLE VIRUSES IN CUTANEOUS DISEASES OF UNKNOWN ETIOLOGY

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The present report deals primarily with the application of a recently developed experimental method to the etiologic problems of a group of cutaneous diseases the causes of which are unknown or in dispute. Most of the clinical material included in this study came from cases of psoriasis, pityriasis rosea and lichen planus. The experimental investigation of 7 cases of pemphigus vulgaris is the subject of a separate communication¹

The methods of mycology and bacteriology have been extensively employed in attempts to determine the causes of the previously mentioned cutaneous diseases, but to date their origin remains obscure. It was therefore determined to reinvestigate the conditions by means of the technic of egg inoculation which was developed by Goodpasture² and his co-workers for the study of filtrable viruses and other infectious agents. This method utilizes the embryonic chick and its enveloping membranes as an experimental animal. The advantages of the method are apparent from the fact that a great variety of pathogenic microorganisms have already been successfully cultivated in the chorioallantoic membrane of the developing chick. Numerous viruses, bacteria and fungi are included in the list. The freedom of the embryo from bacteria and other infectious agents, as well as from previous sensitizations, especially recommends the technic as an approach to etiologic problems in which microbic action or products may play a part. The embryo has a high degree of susceptibility, which is not shared by the adult of the species as regards the majority of the parasites that have been cultivated in the chick embryo. It was assumed, therefore, that if any of the dis-

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1 Markham, F S, and Engman, M F, Jr. LXXXVI—An Inquiry into the Cause of Pemphigus. Is It a Virus Disease? *Arch Dermat & Syph* 41:78 (Jan) 1940

2 Goodpasture E W. Some Uses of the Chick Embryo for the Study of Infection and Immunity, *Am J Hyg* 28:111, 1938

eases concerned in the present undertaking were of virus origin the developing egg might offer a suitable medium for their demonstration and study

METHOD AND MATERIALS

Fertile eggs were incubated for nine to twelve days at 38 C, after which the chorioallantoic membrane was exposed by removing a small segment of the shell and shell membrane. After inoculation the opening was closed with a sterile cover glass and sealed with a mixture of petrolatum and paraffin. Inoculated eggs were incubated at 35 C for four to ten days, during which time the membranes were observed for evidences of infection.

In so far as possible all patients selected for study had early active stages of disease. Biopsy specimens were finely minced with curved iris scissors and ground in a sterile mortar with powdered pyrex glass. The resulting pulp was taken up in 3 to 5 cc of sterile saline solution or broth and allowed to stand until the gross particles settled out. The supernatant fluid was used for inoculations. Portions of 0.05 to 0.1 cc of such preparations, whole blood, serum, spinal fluid or fluid from blisters, were usually inoculated onto the chorioallantoic membrane of each of three to six eggs.

Some specimens were taken from psoriatic lesions, after removal of the superficial scales, by clipping out small bits of epithelium, such as are used for skin grafts, with curved iris scissors. Two or three of these fragments were placed on the membrane of each of three or more eggs.

Specimens of skin were taken after light superficial sterilization with dilute tincture of iodine (approximately 0.1 per cent).

Tissues for histologic examination were fixed in Zenker's solution (prepared with acetic acid), embedded in paraffin and stained with hematoxylin and eosin or with eosin and methylene blue.

RESULTS

Pityriasis Rosca—Specimens from 15 patients were examined. Biopsy material from 5 patients and blood from 10 others were inoculated onto egg membranes. Blood serum from 1 patient was injected in 0.03 cc amounts intracerebrally in four white mice (Buffalo strain).

Although some of the specimens were carried through three to five serial transfers on the chorioallantoic membrane, no evidence of infection either gross or microscopic appeared in the inoculated chick tissues. All the mice remained symptomless during an observation period of six weeks.

Psoriasis—Specimens from 19 patients were examined. Biopsy material from 6 patients, clippings of skin from 8 and blood serum from 3 others were inoculated onto the chorioallantoic membrane of developing eggs. Suspension of triturated scales and scrapings from psoriatic lesions of 2 patients were inoculated onto the scarified corneas of rabbits, one animal being used for each specimen.

Although some of the specimens were given three to six serial passages on the chick membrane, none of the inoculations resulted in

the appearance of lesions differing from those sometimes seen on inoculated or uninoculated control membranes. No vesiculation, keratitis or other manifestation of disease followed the corneal inoculation of the rabbits.

Lichen Planus—Specimens from 11 patients with this disease were examined. Biopsy material from 6 patients, blood serum from 4 and spinal fluid from 2 were inoculated onto the chorioallantoic membranes of developing eggs.

Several of the specimens were subjected to serial passages on the egg membrane, in some instances as many as six times, but in no case did distinctive lesions either gross or microscopic appear on the inoculated membranes.

Other Diseases—Spinal fluid from 1 and blood serum from 2 patients with lupus erythematosus, blister fluid from 1 with erythema bullosum, blood serum from 1 with erythema multiforme, whole blood from 1 with lymphatic leukemia and 1 with aplastic anemia, and biopsy specimens from 1 patient with mycosis fungoides and 1 with granuloma inguinale were inoculated onto the chorioallantoic membranes of developing eggs.

None of the materials gave rise to lesions on the inoculated egg membranes.

COMMENT

The susceptibility of embryonic tissues to infectious agents is well known. Not only are the young usually less resistant to a given parasite than the adults of the same species, but there are many instances in which the prenatal animal has been shown to be susceptible to infections to which the postnatal animal is completely resistant. It was therefore assumed that the chances of demonstrating unknown viruses or other infectious agents would be greatly increased by the use of the developing chick as an experimental animal for the study of cutaneous diseases. Moreover, since the embryonic chick lacks the normal microbic flora and fauna of the adult, the risk of encountering misleading spontaneous infections would be considerably lessened. Finally, the ectodermal origin of the exposed surface of the chorioallantoic membrane was thought to be an additional point in favor of the use of the embryonic chick in the experimental investigation of cutaneous diseases.

In spite of these advantages I was unable to detect the presence of filtrable viruses or other infectious agents in any of the specimens examined by this method. It should be pointed out, however, that the failure to demonstrate an infectious agent by the inoculation of experimental animals is not conclusive proof of noninfectious causation. Such cutaneous diseases as verruca vulgaris and herpes zoster have not been

reproduced successfully in laboratory animals. Nevertheless, reproduction of these diseases by the inoculation of human volunteers with filtrates, together with the characteristic cytologic changes in the lesions, argues strongly for their virus causation. With the possible exception of pityriasis rosea, this type of evidence is lacking in the cutaneous diseases studied in this investigation. On the basis of clinical, histologic and epidemiologic evidence, as well as the experimental data herewith reported, I am inclined to assume that the cutaneous diseases examined in the present study are of noninfectious origin.

PITYRIASIS ROSEA

REVIEW OF THE LITERATURE AND REPORT OF TWO HUNDRED
AND NINETEEN CASES, IN THIRTY-EIGHT OF WHICH
CONVALESCENT SERUM WAS USED

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I INCIDENCE

Nékám¹ observed pityriasis rosea in 4 per cent of 100,000 cases of cutaneous disease, while Stelwagon,² in 123,746 cases collected by the American Dermatological Association from 1878 to 1887, found the disease in only 0.057 per cent. MacLeod³ found 3 cases of pityriasis rosea per thousand cases of cutaneous diseases in children under 14 years of age observed at the Victoria Hospital. Graham Little⁴ saw 6.7 cases per thousand in a dermatologic clinic for adults and children and 4.7 per thousand in a children's clinic. Benedek⁵ quoted statistics from thirteen authors. The frequency of pityriasis rosea in Leipzig was 0.52 per hundred and in Vienna, 1.67 per hundred cases of cutaneous diseases. The frequency index (cases per month) was 0.54 for New York city and 9.7 for Berlin. Bolam⁶ found that pityriasis rosea comprised 0.3 per cent of all dermatoses, Crocker,⁶ 0.4 per cent, Kogoj and Farkas,⁷

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University

Read at the Sixty-Second Meeting of the American Dermatological Association, Inc., Monte-Bello, Quebec, Canada, June 1, 1939

1 Cited by Little⁴

2 Stelwagon, H. W., (a) cited by Little,⁴ (b) *Diseases of the Skin*, Philadelphia, W. B. Saunders Company, 1914, p. 203

3 In discussion on Little⁴

4 Little, E. G. G. Discussion on Pityriasis Rosea, *Proc. Roy. Soc. Med.* 7.121, 1914

5 Benedek, T. Statistische Untersuchungen zur Kenntnis der Pityriasis rosea. *Gibert. I. Häufigkeit, Geschlecht, Lebensalter*, *Arch. f. Dermat. u. Syph.* 170:581, 1934

6 Crocker, H. R. *Diseases of the Skin*, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1903, p. 408

7 Kogoj, F., and Farkas, K.: Clinical Contribution on Pityriasis Rosea, *Urol. & Cutan. Rev.* 36:451, 1932

0.68 per cent, Glaubersohn,⁸ 0.79 per cent, Pollitzer,⁹ Gray¹⁰ and Adamson,¹¹ each, 1 per cent, Lanz,¹² 2 per cent, and Pick,¹³ 3 per cent. Ullmann,¹⁴ in 1932, stated that the disease was becoming more frequent. The diagnosis of pityriasis rosea was made in 394 (1.29 per cent) of 30,604 new patients seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in 1938.

II AGE

Weiss, Lane and Showman¹⁵ reported that 56.6 per cent of their 380 patients with pityriasis rosea were from 10 to 30 years of age. Most of Towle's¹⁶ patients were from 20 to 30 years old, and Thibierge's,¹ from 15 to 35. Two thirds of Highman's and Rulison's¹⁷ patients were from 20 to 40. Benedek⁵ also found that pityriasis rosea was most common in persons between these ages but that the height of the frequency varied in different places. The majority of Chatschaturjan's¹⁸ 146 patients were from 20 to 35 years old, while most of Kogoj's and Farkas'⁷ patients were about 20. Eighty-seven of Szaboky's¹⁹ 119 patients were from 15 to 40 years old, and 41 of Moingeard's²⁰ 56 patients were from 15 to 35. Glaubersohn⁸ observed that the disease is more frequent in persons between 25 and 30 years of age. Ormsby²¹ stated, "Most of the patients are young (fifteen to forty years of

8 Glaubersohn, S. A. Pityriasis rosea, *Dermat Wchnschr* **93** 1589, 1931.

9 Pollitzer, S. Statistical Report of the American Dermatological Association for the Year 1916, *J. Cutan Dis* **36** 294, 1918.

10 Gray, (a) cited by Little,⁴ (b) in discussion on Little⁴.

11 Adamson, H. W., in Allbutt, T. C., and Rolleston, H. D. *System of Medicine*, New York, The Macmillan Company, 1911, vol. 9, p. 395.

12 Cited by Kogoj and Farkas.⁷

13 Pick, E. Pityriasis Rosea, in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1928, vol. 7, pt. 1, p. 401.

14 Ullmann, K. Ueber die Natur der Pityriasis rosea. Ein kasuistisch-kritischer Beitrag, *Dermat Wchnschr* **95** 1153, 1932.

15 Weiss, R. S., Lane, C. W., and Showman, W. A. Pityriasis Rosea, *Arch Dermat & Syph* **15** 304 (March) 1927.

16 Towle, H. P., (a) cited by Weiss, Lane and Showman,¹⁵ (b) Recurrent Pityriasis Rosea, *J. Cutan Dis* **27** 364, 1909.

17 Highman, W. J., and Rulison, R. H. Pityriasis Rosea. A Few Simple Facts, *Arch Dermat & Syph* **7** 163 (Feb) 1923.

18 Chatschaturjan, G. Pityriasis rosea atypica, *Dermat Wchnschr* **93** 1772, 1931.

19 Szaboky, J. Beitrage zur Aetiologie der Pityriasis rosea, *Monatsh f prakt Dermat* **43** 495, 1906.

20 Moingeard, A. Etude sur le pityriasis rose de Gibert, Thesis, Paris, no. 325, 1889.

21 Ormsby, O. *Diseases of the Skin*, Philadelphia, Lea & Febiger, 1934.

age)," and Bolam³ considered pityriasis rosea a disease of youth, but Crocker⁶ had a patient 70 years old, and Thomson and Cumings,²² one 77 years old. Most of the patients of the latter authors were from 6 to 15 years of age. The ages of Savill's³ patients ranged from 11 months to 50 years, and those of Adamson's,¹¹ from 2 to 60 years (the majority being from 15 to 30). The average age of 153 of our patients was 26.8 years. Thirty-eight per cent were from 20 to 35 years old. The youngest patient was 5 years old and the oldest 53.

III SEX

The general opinion is that pityriasis rosea is twice as frequent in women as in men. Weiss, Lane and Showman¹⁵ reported that 65 per cent of their patients were women and 35 per cent, men. This ratio of about 2 women to 1 man was the same for all ages and agrees with the reports of Towle,¹⁰ Thibierge,¹ Moingeard²⁰ and Adamson¹¹ and almost agrees with that of Highman and Rulison¹⁷. However, 67 per cent of Szaboky's¹⁰ 119 patients and 55 per cent of Chatschaturjan's¹⁸ 146 patients were men and 71 per cent of Tandler's²³ 14 patients were men. Benedek,⁵ Little,⁴ Kogoj and Farkas,²⁴ Crocker⁶ and Cunningham²⁵ found the incidence about equal in the two sexes. Fifty-two and a half per cent of Thomson's and Cumings'²² 156 patients and 80 per cent of Kirby-Smith's²⁶ were women. Pernet,³ Glaubersohn,⁸ Oimsby²¹ and Simon²⁷ also found that pityriasis rosea was more frequent in women than in men. Of 199 of our patients 58.25 per cent were women and 41.75 per cent men.

IV RACE

Pityriasis rosea is usually seen in white persons, but the occurrence of this eruption in Negroes has been reported by Weiss,²⁸ Gross,²⁹

22 Thomson, M. S., and Cumings, J. N. Investigations into the Causation of Pityriasis Rosea, *Brit J Dermat* **43**:628, 1931.

23 Tandler, G. Ueber Pityriasis rosea (Gibert), *Arch f Dermat u Syph* **37**:127, 1896.

24 (a) Kogoj, F. Pityriasis Rosea Haemorrhagica, *Dermat Wchnschr* **97**:1261, 1933. (b) Kogoj and Farkas⁷.

25 Cited by Weiss, Lane and Showman¹⁵.

26 In discussion on Hazen, H. H. Pityriasis Rosea. Late Observations on Etiology and Treatment, *South M J* **24**:937, 1931.

27 Simon, C. Quelques reflexions et souvenirs sur le pityriasis rosé de Gibert, *Bull med, Paris* **50**:702, 1936.

28 Weiss, L. Pityriasis Rosea. An Erythematous Eruption of Internal Origin, *J A M A* **41**:20 (July 4) 1903.

29 Gross, E. R. Pityriasis Rosea (Extensive Involvement), *Arch Dermat & Syph* **37**:686 (April) 1938.

Stillians and Benedek³⁰ and Schiller³¹ Howard Fox³² reported on 2,200 cases of cutaneous diseases in white persons and the same number in Negroes. He found pityriasis rosea in 7 (0.318 per cent) white patients and in 6 (0.272 per cent) Negroes. Schamberg³³ reported seeing pityriasis rosea in a mulatto. In discussion of this case, Davis³⁴ said that he and Knowles a few days previously had seen the disease in a mulatto woman. Corson,³⁵ Butterworth³⁶ and Klauder³⁷ observed that papular pityriasis rosea is more frequent in Negroes, and Guequerre³⁸ stated that the eruption is apt to be more severe and extensive in this race. Of the 380 patients seen by Weiss, Lane and Showman³⁹ in St. Louis, 24.2 per cent were Negroes. Of our 219 patients, only 2 were Negroes.

V DURATION

In the first report on pityriasis rosea, Gibert³⁰ stated that the duration was from six weeks to two months, and Simon²⁷ observed that spontaneous healing occurred in six to twelve weeks. According to Ormsby,²¹ "The affection runs its course ordinarily in from four to eight weeks, but may last for several months, if new lesions continue to appear." Adamson¹¹ found that the average duration was from five to eight weeks, and Pernet,³ from three to four weeks. Duhring⁴⁰ and Jamieson⁴⁰ reported cases of "pityriasis perstans," and Weiss, 2 cases in which the lesions appeared and disappeared for over three

30 Stillians, A. W., and Benedek, T. Leukoderma Following Pityriasis Rosea, *Arch. Dermat. & Syph.* **37** 103 (Jan.) 1938.

31 Schiller, A. E. (a) Pityriasis Rosea in a Negro, *Arch. Dermat. & Syph.* **28** 127 (July) 1933, (b) Pityriasis Rosea, *ibid.* **31** 546 (April) 1935.

32 Fox, H. (a) Observations on Skin Diseases in the Negro, *J. Cutan. Dis.* **26** 67, 1908, (b) cited by Weiss, Lane and Showman¹⁵.

33 Schamberg, J. F. (a) A Case of Pityriasis Rosea in a Mulatto, *J. Cutan. Dis.* **27** 267, 1909, (b) in discussion on Friedman. Pityriasis Rosea Urticata, *Arch. Dermat. & Syph.* **26** 757 (Oct.) 1932.

34 In discussion on Schamberg³³.

35 In discussion on Gross²⁹.

36 Butterworth, T. Pityriasis Rosea. Clinical Varieties and Etiology, *Pennsylvania M. J.* **38** 402, 1935.

37 Klauder, J. V. Pityriasis Rosea, with Particular Reference to Its Unusual Manifestations, *J. A. M. A.* **82** 178 (Jan. 19) 1924.

38 Guequerre, J. P., (a) in discussion on Gross,²⁹ (b) Pityriasis Rosea, Associated with Oral Lesions, *Arch. Dermat. & Syph.* **38** 262 (Aug.) 1938, (c) 159 (July) 1938.

39 Gibert, C. M. *Traite pratique des maladies speciales de la peau*, ed. 3, Paris: G. Bailliere, 1860, p. 402.

40 Cited by Butterworth³⁶.

years Vidal ⁴¹ reported a case in which the condition lasted six months, while in Bailey's ⁴² case the skin was entirely clear in twelve days Bronson,¹ Montgomery,²⁵ Crocker,⁶ Phillips,²⁵ Franck,⁴³ Tenneson ¹ and Savill ³ have reported cases in which the condition persisted for several months In Hallopeau's ⁴⁴ case and in Fournier's ⁴⁵ the eruption lasted four years Little had 3 cases in which the condition lasted for only two weeks and several in which it lasted for three weeks, but in 1 it persisted for five to six months He found that the usual duration was from five to six weeks The average duration in our 26 control cases was four and seven-tenths weeks

VI SEASONAL INCIDENCE

There is great variation in the reports in the literature as to the season when pityriasis rosea is most prevalent Adamson ¹¹ found that the seasonal incidence varied from year to year Weiss, Lane and Showman ¹⁵ found pityriasis rosea most frequent in the spring and fall In the series which they compiled from the literature and in their own cases, the incidence was greatest in January, high from September to May and lowest in July Ormsby ²¹ stated that "without question pityriasis rosea is more common in the spring and in the autumn than in other seasons " Most of Towle's ¹⁶ cases occurred in the autumn, and Thomson and Cumings ²² and Little ⁴ encountered most of their cases in October, but 63 per cent of Moingeard's ²⁰ 56 cases and the majority of Bazin's ²⁵ were observed in the spring Kogoj and Farkas ²⁴ encountered the fewest cases in summer and early winter, while Simon's ²⁷ cases were more frequent in warm weather Gibert ³⁰ also observed that pityriasis rosea is most frequent in the hot months, but Little,⁴ Whitfield,⁵ Pernet ³ and Savill ³ noted more cases in the winter Gray ¹⁰ and Whitfield ³ both noticed that there were more cases than usual in the cold damp summer of 1912 Most of the cases reported by Highman Rulison and Fox ^{32b} occurred from December to March Glaubersohn ⁸

41 Vidal, E, (a) cited by Weiss, Lane and Showman, ¹⁵ (b) Du pityriasis circinéet et marginé Description de son mycoderme, le microsporon anomæon (microsporon dispar) Ann de dermat et syph 3:22, 1882

42 Bailey, H Pityriasis Rosea Report of a Case with Lesions of the Palms and Soles, Arch Dermat & Syph 32:104 (July) 1935

43 Franck, G Pityriasis rosé de Gibert atypique, Schweiz med Wchnschr 12 709, 1931

44 Hallopeau, (a) cited by Little, ⁴ (b) cited by Friedman Pityriasis Rosea Urticata Arch Dermat & Syph 26 757 (Oct) 1932, (c) cited by Greenhouse, C, and Cornell, V H Pityriasis Rosea Report of a Case Showing a Gigantic Herald Plaque with Unusual Manifestations, ibid 28:823 (Dec) 1933

45 Cited by Friedman Pityriasis Rosea Urticata Arch Dermat & Syph 26: 757 (Oct) 1932

found pityriasis rosea least frequent in the fall. Little¹ noticed a rise in the frequency of pityriasis rosea in July, October and December. Szaboky,¹⁰ Fiocco²⁵ and Ciocker⁶ noted no seasonal variation. In 78 (38 per cent) of 203 of our cases the condition started in the fall, in 59 in the winter, in 38 in the spring and in 28 in the summer.

VII SYSTEMIC SYMPTOMS AND ETIOLOGIC BACKGROUND

Ormsby²¹ stated, "Mild constitutional disturbance exhibited as headache, moderate elevation of temperature, congestion of the fauces and slight enlargement of submaxillary and cervical glands may accompany an acute widespread eruption." He has found that many patients with pityriasis rosea have light hair and delicate skins and have been enfeebled by physical fatigue and overwork in school. Simon²⁷ also found pityriasis rosea more frequent in patients with fine skin and blond hair. In 42.3 per cent of Gourvitch's⁴⁶ 85 cases and in 50 per cent of Szaboky's¹⁰ cases there were prodromal symptoms of malaise, headache, chills and fever. Thomson and Cummings²² observed slight fever (maximum 100 F) in 6 of 18 cases, in 2 of them there was arthralgia and in 2 dyspepsia. Little¹ stated the belief that general glandular enlargement occurs in the majority of cases. MacLeod³ said that general symptoms are not infrequent, but the general health of Adamson's¹¹ patients was good. Alderson⁴⁷ noted definite, severe nervous stress from prolonged, excessive mental work, worry or actual shock in 10 of 11 cases studied. Only 2 of our 219 patients complained of any prodromal symptoms. One had malaise and sore throat, and 1 had vomiting and diarrhea.

VIII RELATION OF INFECTION OF THE TONSILS TO PITYRIASIS ROSEA

Pernet,³ Dore³ and MacLeod³ frequently found involvement of the tonsils and general glandular enlargement in patients with pityriasis rosea. Twelve of Owen's⁴⁸ 30 patients had infection in the upper part of the respiratory tract or in the tonsils. About 50 per cent of Mestchersky's⁴⁰ patients complained of sore throat. Wile⁴⁸ declared that

46 Gourvitch, E. I. Sur la clinique, la pathogénie et le traitement du pityriasis rose de Gibert. *Pityriasis rosea* Gibert, *Ann de dermat et syph* 7 488, 1936.

47 Alderson, H. *Pityriasis Rosea*. Clinical Observations, *J Cutan Dis* 32 353, 1914.

48 Cited by Hazen, H. H. *Pityriasis Rosea*. Late Observations on Etiology and Treatment, *South M J* 24 937, 1931.

49 Mestchersky, G. Contribution a l'étiologie du pityriasis rosé de Gibert, *Bull Soc franç de dermat et syph* 33 148, 1926.

pityriasis rosea apparently occurs only in persons who still have their tonsils, and he often found enlarged lymph glands in patients with this disease. Haspel⁵⁰ had 6 patients with pityriasis rosea and infected tonsils. In each case the eruption disappeared in one to four days after tonsillectomy. Hazen⁵¹ found the tonsils or lymphoid structures of the throat diseased in 94 per cent of 70 patients with pityriasis rosea. Four patients had recurrent attacks of the eruption, each of which was associated with a definite follicular tonsillitis. The diseased tonsils or lymphoid tissue in the throat was present in only 20 per cent of 300 control patients with other cutaneous diseases. From these observations Hazen assumed that the portal of entry in pityriasis rosea probably is the tonsils. An exactly opposite opinion was expressed by Weiss,⁵² who said that there is no direct association between pityriasis rosea and diseased tonsils, and by Kirby-Smith^{53a} and Highman,^{53b} who both stated that they had never found infections of the throat associated with pityriasis rosea. Only 5 of Thomson's and Cuming's²² 18 patients showed any faucial congestion, only 1 had symptoms referable to the throat, and only 3 had any adenopathy. In only 2 of these 3 were the cervical glands enlarged. None of our patients complained of sore throat, but the throat was examined in only a few.

IX. CONTAGION AND OCCURRENCE OF MORE THAN ONE CASE IN THE SAME HOUSEHOLD

Lord⁵³ reported the simultaneous appearance of pityriasis rosea in 2 members of his own family. His son had a typical generalized pityriasis rosea, and his wife, a characteristic herald plaque. In a review of the literature he cited 18 other instances of pityriasis rosea apparently occurring as a result of close association. Haas⁵⁴ had pityriasis rosea himself, and a few days later the same disease developed in his wife, his mother, his baby and the baby's nurse. Fourteen days after he took care of a patient with pityriasis rosea, a herald patch developed at the site of a trauma on Edelston's⁵⁵ own skin. Zeisler¹ had pityriasis rosea himself, and two weeks later his wife had the same eruption. Kurtz

50 Haspel, K. L. Angaben zur Aetiologie der Pityriasis rosea, *Dermat Wehnschr* **102**:357, 1936.

51 Hazen, H. H. Pityriasis Rosea. Late Observations on Etiology and Treatment, *South M J* **24**:937, 1931.

52 Weiss, R. S., (a) in discussion on Hazen,⁵¹ (b) in discussion on Weiss, Lane and Showman¹⁵

53 Lord, L. W. Etiology of Pityriasis Rosea, *Arch Dermat & Syph* **26**:981 (Dec) 1932.

54 Haas, A. Identität von Herpes tonsurans und Pityriasis circinata (?), *Berl klin Wehnschr* **17**:259, 1882.

55 Cited by Thomson and Cumings²²

and Davis,⁵⁶ medical students who worked but did not room together, contracted pityriasis rosea within one week of one another. Weiss, Lane and Showman¹⁵ reported 2 instances of pityriasis rosea in the same family, in one family a girl and her brother had the disease, and in the other, a woman and her son. Two cases in the same household have been reported also by Photinos,⁵⁷ Fordyce,⁵⁸ Peroni,¹⁸ Horand,¹ Crocker,⁹ Fox⁵⁹ and Wile.²⁵ Butterworth³⁰ stated that he had seen 2 or more cases in the same household on more than twenty occasions, but none of Hazen's⁴⁰ 150 cases were in the same home. Little⁴ found only 1 instance of infectivity in 174 cases. Pernet³ found no instances of contagion in his series of cases, and this was also our experience.

X ETIOLOGIC AGENTS BACTERIA FUNGI AND THE WEARING OF NEW, UNWASHED OR DAMP CLOTHING

In 1882 Vidal^{41b} discovered a microsporion in lesions of pityriasis rosea. This finding was confirmed by Ferrari⁴⁸ and Du Bois,⁶⁰ and Gougerot⁶¹ stated that these spores are the cause of the disease and that they are similar to blastomycetes. In 1889 Kaposi⁴⁸ and Newman⁴⁸ discovered mycelia. Photinos⁵⁷ found spores in each of 4 cases studied. They were also found by Covisa⁶² and Nekám.¹ Joyeux and Burnier⁶¹ demonstrated spores in scales from a patient with typical pityriasis rosea after injections of tréparsol (the sodium salt of 4-formylamino-4-hydroxyphenylarsenic acid). Joyeux, Burnier and Duché⁶⁴ observed spores in 28 of 30 cases but were unable to cultivate them or to produce the disease by injecting solution made with the scales into other patients. Thomson and Cummings²² and Whitfield³ stated the belief that these so-called spores are merely fluid artefacts. Brocq⁶⁵

56 Kurtz, F. H., and Davis, J. B. Pityriasis Rosea. An Account of Suggested Contagiousness and of Attempted Experimental Transmission. *Arch. Dermat. & Syph.* **28** 13 (July) 1933.

57 Photinos, P. Beitrag zur Natur der Pityriasis rosea, *Dermat. Ztschr.* **68** 187, 1934.

58 Fordyce, J. A. A Case of Pityriasis Rosea, *J. Cutan. Dis.* **14** 356, 1896.

59 Fox, G. H. Pityriasis Rosea, *J. Cutan. Dis.* **16** 340, 1898.

60 Du Bois. Parasite cryptogamique des dermatoses erythemato-squameuses du type pityriasis rose de Gibert, *Ann. de dermat. et syph.* **3** 32, 1912.

61 Gougerot, H. Traitement du pityriasis rose de Gibert par l'éosine, *Bull. Soc. franç. de dermat. et syph.* **44** 1708, 1937.

62 Covisa, J. S. Pityriasis rosea Gibert, *Dermat. Wchnschr.* **56** 115, 1913.

63 Joyeux and Burnier. A propos d'un cas de pityriasis rose, *Bull. Soc. franç. de dermat. et syph.* **36** 1054, 1929.

64 Joyeux, Burnier and Duché. Recherches sur la nature mycosique du pityriasis rosé, *Bull. Soc. franç. de dermat. et syph.* **37** 1128, 1930.

65 Brocq, B., (a) cited by Simon,²⁷ (b) Note sur la plaque primitive du pityriasis rosé de Gibert, *Ann. de dermat. et syph.* **8** 615, 1887.

was of the opinion that the disease is passed along by an insect bite, probably that of a flea, but Simon²⁷ lately obtained a history of flea bites from his patients and stated the belief that pityriasis rosea is due to a filtrable virus. Thomson and Cumings²² agreed with this opinion. Benedek⁶⁶ considered pityriasis rosea due to a constant endoparasitism of *Schizosaccharomyces hominis* and produced by a hematogenous infectious route. He stated the belief that the parasite is carried by the blood into skin which is already alleigized and that it then decomposes in the lesion itself through the immune powers of the macrophage. He considered this theory proved by the presence of the primary mycotic focus, the specific allergy and the parasite in the blood and cutaneous lesions during the exanthem. He attributed the inability to transmit or produce the disease to the fact that every person, because of the constant endoparasitism, has an immunity against a superimposed infection due to *Schizosaccharomyces*. Thomson and Cumings²² were unable to find Benedek's organisms in cultures of blood or blister fluid from the herald patch, and Pernet³ could find no fungi of any type in the scales. Oppenheim⁶⁷ reported that pityriasis rosea is due to a ringworm organism which enters through the herald patch, from which spores appear in the blood, and that the secondary lesions are due to embolic thrombi in the fine capillaries of the skin. Hebra⁶⁷ and Kaposi⁴⁸ have also stated the belief that the disease is due to a ringworm-like parasite.

Many German authors especially Lassar,⁶⁸ have declared that pityriasis rosea is due to the wearing of new, unwashed or damp garments. Veiel⁶⁹ reported several cases in which the disease apparently occurred after the wearing of new or damp linen, and Wise and Sulzberger⁷⁰ have commented on the frequency of this association. Parkhurst²⁵ often observed in the history of a patient that the disease occurred after wearing clothing which had been stored in a damp, dark place, and he expressed the opinion that it is due to contact with some organism which grows in such places. Kogoj and Farkas⁷ reported a case in which the herald patch on the left knee appeared shortly after the patient had worn new trousers over short underwear and another case in which the eruption appeared two weeks after the wearing of a sweater which had lain in a wardrobe during the summer. Heath⁷

66 Benedek, T. *Schizosaccharomycosis. II. Clinical (Mycotic) Forms, Pityriasis Rosea of Gibert, Its Etiology and Pathogenesis*, Arch. Dermat. & Syph. 26:397 (Sept.) 1932.

67 Cited by Lord²³.

68 Lassar, O. *Ueber die Natur der Pityriasis rosea*, Deutsche med. Wchnschr. 18:469, 1892.

69 Veiel, F. *Zur Kenntnis der Pityriasis rosea*, Dermat. Ztschr. 62:91, 1931.

70 Wise, T., and Sulzberger, M. B. *Year Book of Dermatology and Syphilology*, Chicago: The Year Book Publishers, Inc., 1931, p. 154, 1934, p. 565.

reported a case in which pityriasis rosea occurred in a boy two days after he had worn a fresh flannel vest while running a race. Thomson and Cumings⁷² stated the belief that the herald patch is almost always on the trunk because there the clothes most closely touch the body. Le Damany⁷³ expressed the unique opinion that pityriasis rosea is a tuberculid. Only 32 (19.05 per cent) of the 168 of our patients gave a history of wearing new or damp clothing shortly before the appearance of the eruption. In obtaining this history, however, we questioned the patient only about clothing worn over the site of the herald patch, and this may account for the relatively low percentage.

XI LABORATORY INVESTIGATIONS

Milian and Perin⁷¹ cultured streptococci from dyshidrotic vesicles on the hands of a boy who had bullous impetigo and pityriasis rosea and questioned whether the latter disease was not also due to a streptococcus. In all of 20 patients with pityriasis rosea Périn⁷² obtained a positive reaction with a streptococcus vaccine. Three normal persons and 8 patients with other dermatoses gave a negative reaction. A year later, with the assistance of Michaux and Cottet, Périn⁷³ confirmed this work. Gourvitch⁷⁴ also stated the belief that pityriasis rosea is of streptococcic origin. Of his 55 patients only 4 failed to react to intradermal injections of streptococcus vaccine, while 50 gave no reaction to staphylococcus vaccine. A series of control patients all gave negative reactions to streptococcus vaccine. Examination of the blood of 28 of his patients showed lymphocytosis in 8 and eosinophilia in 9. Examinations for tinea, trichophyton tests and injections of a solution made from the scales into normal men and animals all gave negative results. Examination of the blood of Milian's⁷⁴ patient revealed 7 per cent eosinophils. Thomson and Cumings⁷² found no consistent organisms in cultures of smears from the throat or feces, and all examinations of the urine gave negative results. They discovered a "definite tendency towards leucopenia with relative lymphocytosis." With intradermal injections of an extract of scales from a herald patch in saline solution, they obtained only two negative reactions in 13 healthy persons, one negative in 5 patients with other dermatoses and only one positive and two very weakly positive reactions in 10 patients with pityriasis rosea.

71 Milian, G., and Perin, L. Trisyndrome, *Bull. Soc. franç. de dermat. et syph.* 38 852, 1931.

72 Perin, L. Pityriasis rose de Gibert et intradermo-reactions au vaccin streptococcique, *Bull. Soc. franç. de dermat. et syph.* 35 795, 1928.

73 Perin, L., Michaux, L., and Cottet, J. Intradermo-reactions streptococciques dans le pityriasis rosé de Gibert, *Rev. franç. de dermat. et de vénéréol.* 5 3, 1929.

74 Milian, G. Pityriasis rosé de Gibert à croûtes impétiginiformes, *Rev. franç. de dermat. et de vénéréol.* 5 15, 1929.

XII ATTEMPTS TO PRODUCE PITYRIASIS ROSEA EXPERIMENTALLY

Wile⁷⁵ produced a blister on a herald plaque by the application of a cantharides plaster and injected fluid from the blister percutaneously and by scarification. After several failures, he was finally able to produce an explosive form of pityriasis rosea in 3 patients who were inoculated and in 1 who was scarified. Owens²⁵ and Thomson and Cumings²² were unable to produce pityriasis rosea by inoculation of scales from the lesions. Many other attempts also have been unsuccessful. Kurtz and Davis⁵⁶ injected intradermally filtrates of a saline solution suspension of scrapings from a herald spot into patients with acute pityriasis rosea and into others convalescing from the disease. In 15 of 18 patients in four hours there was a local, circumscribed hyperemia, which disappeared in twenty-four hours. There were no positive reactions in definitely convalescent patients or in healthy persons, and no lesions resembling pityriasis rosea developed. These authors also removed typical secondary lesions of pityriasis rosea with a curet and made a suspension of them in Ringer's solution, which they injected intradermally into clear areas of their own skin while they had the eruption and into the skin of 2 healthy persons and of 2 rabbits. No local reaction occurred in themselves, in the healthy persons or in the rabbits.

XIII LOCATION OF ERUPTION

Lesions of pityriasis rosea may occur on any part of the body, but they are most frequent and numerous on the trunk. In Weiss's, Lane's and Showman's¹⁵ cases, the trunk was involved in 72.2 per cent, the arms in 39.3 per cent, the thighs in 33.4 per cent, the neck in 17.3 per cent, the face in 7.9 per cent, the shoulders in 7.3 per cent, the legs in 4.4 per cent, the feet in 3 per cent, the buttocks in 2.3 per cent, the forearms in 2.3 per cent, the axillas in 2.1 per cent, the hands in 1.8 per cent and the genitocrural region in 1.2 per cent. In almost 10 per cent the eruption was generalized. Little⁴ had a patient with lesions on the whole surface of the skin except the hands and feet. Dühring,¹ Little,⁴ Howard Fox^{32b} and Chatschaturjan¹⁸ have reported cases in which there were lesions on the penis. In 179 of our patients the eruption was on the trunk in 91 per cent, the extremities in 86.6 per cent, the neck in 59.8 per cent, the face in 19.6 per cent and the scalp in 3.9 per cent.

XIV LOCALIZED FORMS

Dore¹ and Klauder⁷⁶ expressed the opinion that localized forms of pityriasis rosea are not uncommon and tend to last longer than a gen-

⁷⁵ Wile, U. J. Experimental Transmission of Pityriasis Rosea, Arch. Dermat. & Syph. 16:185 (Aug.) 1927.

⁷⁶ In discussion on Weiss, Lane and Showman¹⁵.

elialized eruption Butterworth ¹⁶ observed that localized pityriasis rosea usually is seen in the groins and in the axillas He mentioned the so-called "inverted pityriasis rosea" in which the lesions are limited to the extremities Pityriasis rosea limited to the face and neck has been reported by Little,⁴ Mongeard,²⁰ Photinos ⁷⁷ and Towle ^{16a} Szaboky,¹⁹ Mongeard ²⁰ and Klaudei ¹⁷ have described unilateral distribution of pityriasis rosea Little ¹ reported a case with lesions only on the thighs and another with the eruption limited to the right hip, buttock and thigh Costello ⁷⁷ reported an eruption of pityriasis rosea exactly limited to an area covered by bathing trunks and to the axillas and the upper inner aspect of the arms, which appeared about six months after acquiring a deep tan on the rest of the body He also mentioned a woman who had been treated with roentgen rays for a dermatosis involving the left side of the chest Later profuse pityriasis rosea developed, but the previously irradiated areas were completely spared In 179 of our patients the eruption was limited to the neck in 2 and to the abdomen in 1

XV TYPES OF LESIONS

In the majority of cases of pityriasis rosea the eruption consists of macules, but often papules and occasionally other lesions are present Benedek ⁷⁸ described ten types of lesions seen in pityriasis rosea macules, papules, maculopapules, urticarial papules, vesicles, lichenoid lesions, small red hemorrhagic spots, lesions resembling lichen planus, lesions like erythema multiforme and lesions resembling chronic lichenoid pityriasis On examination of 1,556 cases in the literature, he concluded that there is only one typical lesion, the macule In the cases reported by Weiss, Lane and Showman ¹⁵ macules were present in 76.1 per cent, papules in 7.9 per cent, mixed papules and plaques in 13.1 per cent and circinate lesions in 2.7 per cent Vesicles were seen in 2 cases

XVI ATYPICAL FORMS

Fourteen (9.5 per cent) of Chatschaturjan's ¹⁸ 146 cases of pityriasis rosea were atypical In one group the eruption started with maculopapular lesions, the size of a pinhead, which were more numerous on the neck and chest than on the trunk In the second group first there was severe itching, which was followed by an urticarial and papulovesicular eruption with infiltrated lesions, some of which resembled scabies and some, erythema multiforme In both groups typical lesions appeared after a few days Weiss, Lane and Showman ¹⁵ commented on the fact

⁷⁷ Costello, M. J. Pityriasis Rosea Sparring Tanned Areas of the Skin (Bathing Trunk Distribution), Arch Dermat & Syph **38** 75 (July) 1938

⁷⁸ Benedek, T. Statistische Untersuchungen zur Kenntnis der Pityriasis rosea Gibert, Acta dermat-venereol **17** 151, 1936

that pityriasis rosea has multiform lesions, and Klauder⁷⁹ described nine distinct varieties. Wirz,¹² Schweitzer⁴⁰ and Kogoj^{21a} have reported cases of pityriasis rosea with small red hemorrhagic points, and Klauder⁷⁶ has noticed a recent increase in "pityriasis rosea hemorrhagica." Vesicular pityriasis rosea has been described by Little,⁴ Fox²⁵ and Wile²³. Weiss^{52b} and Butterworth⁶ expressed the opinion that this type lasts longer than the common type. Ullmann¹⁴ had 1 patient with vesicles on the soles, 1 with hyperkeratotic eczematoid changes on the soles, toes and finger tips and deep, scaly infiltrations on the palms, and another with vesicles which later became pustules. He said that he had seen more atypical and severe forms lately. Sobel⁸⁰ presented a patient with a generalized eruption of pink macules, some of which were topped with vesicles, and Weiss²⁸ reported on a patient who had small plaques capped with a clear vesicle. Becker and Ritchie⁸¹ had a patient with pityriasis rosea, with papules and superficial vesicles on the trunk, arms and thighs. They commented that there are microscopic vesicles in many cases and that probably macroscopic vesicles are merely an exaggeration of this process. Klauder⁷⁶ said that vesicular pityriasis rosea is unusual. Adamson¹¹ stated that the vesicular type is especially frequent in infants and children, but this is not the general opinion, although Weiss^{52b} has found that pityriasis rosea in children is chiefly papular and vesicular. Blaschko's⁴⁰ patient had bullae on the mucous membranes. Kiess^{82a} described 2 cases of pityriasis rosea with many pustular lesions, in the first the pustules followed bullae, and in the second the lesions were pustular from the onset. In 2 cases reported by Weiss, Lane and Showman¹⁵ and in Becker's and Ritchie's⁸¹ case, the eruption at first resembled varicella and later became typical of pityriasis rosea. Kiess^{82b} reported 2 cases of "pityriasis rosea pustulocrustosa." Milian⁷⁴ described a case of pityriasis rosea with medallions and papules, many of which were covered with yellow dry, adherent crusts. Little⁴ had a patient with an itchy, almost universal eruption which was followed by marked scaling and another patient with an extensive eruption consisting of many extremely itchy follicular maculopapules. Howard Fox's^{32b} patient also had follicular papules. Vidal^{41b} first described "pityriasis circiné et marginé," which is now generally accepted as a type of pityriasis rosea characterized by its long duration.

79 In discussion on Friedman⁸⁵

80 Sobel, N. Pityriasis Rosea with Vesicles, Including the Face, Arch Dermat & Syph 38:466 (Sept) 1938

81 Becker S W, and Ritchie, E B. Pityriasis Rosea (Vesicular), Arch Dermat & Syph 23:779 (April) 1931

82 Kiess O. (a) Weiterer Beitrag zur Kenntnis der Pityriasis rosea palmaris et plantaris. Dermat Wchenschr 96:368 1933. (b) Pityriasis rosea, Pityriasis rosea et pustulo-crustosa, ibid 92:945, 1931

Dühring⁸³ and Colcott Fox⁸⁴ reported cases of "pityriasis rosea maculata et circinata," and Darier,²⁵ Pimple,²⁵ Nékám¹ and Klauder⁸⁷ reported cases of "pityriasis rosea gigantea," with palm-sized symmetric plaques and circles on the body. Friedman⁸⁵ presented a case with extremely itchy, red, raised urticarial lesions. Both Savill³ and Little⁴ had cases of this type which was first described by Hallopeau^{44b} in 1906, as the "forme oitée," and later by Vornier⁴⁵. Dore³ has found that in many patients the eruption is urticarial. According to Butterworth,³⁶ the urticarial factor is most marked at the onset of the eruption. Stokes⁷⁹ and Gourvitch⁴⁶ agreed that a highly nervous patient has a much more florid urticarial type of pityriasis rosea. None of our patients had atypical lesions except 2 who had several urticarial wheals.

XVII LESIONS ON THE SCALP AND FACE

Butterworth³⁶ stated that "The only recorded instance in which pityriasis rosea involved the scalp in an adult was Gager's case in a female, age 35,"⁴⁰ but Kumer,¹² Weiss,²⁸ Horand,¹ Adamson,¹¹ Haxthausen,⁸⁶ Fuhs,¹² Kerl,¹² Oppenheim,¹² Pick,¹³ Dufke¹² and Balina⁸⁷ have described lesions on the scalp. Cole⁸⁸ stated that there is greater tendency for pityriasis rosea to involve the scalp in children than in adults, and Haxthausen asserted that the scalp is almost always involved in pityriasis rosea in children. In the first case reported by Weiss, Lane and Showman¹⁵ the lesions first appeared on the face and later on the scalp, and both these areas were involved in their fourth case. Guequerre^{78a} commented that in the last few years he had observed several patients with lesions on the neck and scalp, and Knowles⁸⁵ agreed that recently he has noticed lesions extending to the neck and the lower part of the face. Barney's⁸⁹ patient had many lesions on the face and scalp, and Montgomery and Culver,⁹⁰ Stowers,²⁵ Stillians and Benedek⁸⁰

83 Dühring, L. A. Pityriasis Maculata et Circinata, *Am J M Sc* **80** 359, 1880

84 Fox, C. On the Disease of the Skin Named Pityriasis Maculata et Circinata, *Lancet* **2** 485, 1884

85 Friedman. Pityriasis Rosea Urticata, *Arch Dermat & Syph* **26** 757 (Oct) 1932

86 Haxthausen, H. Pityriasis Rosea of the Scalp, an Almost Invariable Location of the Disease in Children, *Brit J Dermat* **39** 141, 1927

87 Balina, P. L. Pityriasis rosada de Gibert familiar. Tres casos simultaneos, consideraciones, *Semana méd* **2** 1169, 1927

88 In discussion on Barney, R. E. Pityriasis Rosea Involving the Scalp, *Arch Dermat & Syph* **25** 190 (Jan) 1932

89 Barney, R. E. Pityriasis Rosea Involving the Scalp, *Arch Dermat & Syph* **25** 190 (Jan) 1932

90 Montgomery, D. W., and Culver, G. D. Pityriasis Rosea. Two Unusual Cases, *Arch Dermat & Syph* **12** 257 (Aug) 1925

Sobel⁸⁰ and Gross²⁰ have presented patients with lesions on the face. In Friedman's⁸⁵ patient the herald plaque was on the chin, and the generalized eruption started on the face and spread downward. Szaboky¹⁰ had a patient with lesions on the eyelids. Klauder⁷⁹ stated the belief that lesions are rare on the face but not on the neck. We were surprised at the large number of our patients who had lesions on the face (19.55 per cent) and on the scalp (3.91 per cent) and agree with the comments of several authors that lesions on these areas have become more frequent recently.

XVIII LESIONS ON THE HANDS AND FEET

Szaboky¹⁰ stated that pityriasis rosea never occurs on the hands and feet, but cases in which there were lesions on the palms and soles have been reported by Rille,¹² Ullmann,¹⁴ Schamberg,¹² Conrad,¹² Balban,¹² Little,⁴ Benedek,⁹¹ Fessler,¹² Kerl,¹² Kren,¹² Oppenheim,¹² Kiess,⁸² Volk,¹² Mongeard,²⁰ Parkhurst,⁹² Klauder,⁹³ Stowers²⁵ and Rosen.⁹⁴ Weiss, Lane and Showman¹⁵ reported that in 1.8 per cent of their cases the lesions were on the hands and in 3 per cent on the feet. In 1 of their cases the lesions were on the palms and soles, resembling those of pompholyx. Duhring⁴⁰ and Fox²⁵ reported on patients with lesions on the dorsa of the hands, and Wright's⁹⁵ and Mongeard's²⁰ had lesions on the dorsa of the feet and in the webs of the fingers. Kogoj and Farkas⁷ observed that the soles are less often affected than the palms. Combes described five forms in which pityriasis rosea appears on the hands and feet: (1) discrete, scaly red plaques, (2) livid red, slightly elevated and infiltrated maculopapules, with tiny vesicles on the thin-skinned portions of the fingers and toes, (3) scaly red patches on the inner surfaces of the palms and soles intermingled with vesicles, (4) closely arranged dyshidrotic vesicles resembling sago grains, and (5) universal redness and scaling of the palms and soles. He reported a case⁹⁶ in which deep, dusky red lesions with a collarette of scales, which resembled syphilids, were on the palms and soles and papules were on the forearms, wrists and dorsa of the hands. Bailey⁴² reported a typical case of pityriasis rosea in which there were similar

91 Benedek, T. Bezüglich Pityriasis Rosea. *Gibert, Dermat. Wchnschr.* 86:90, 1928.

92 In discussion on Schiller.^{31a}

93 Klauder, J. V. Pityriasis Rosea, *Arch. Dermat. & Syph.* 19:523 (March) 1929.

94 In discussion on Sobel.⁸⁰

95 Wright, C. S. Pityriasis Rosea of Unusual Distribution, *Arch. Dermat. & Syph.* 26:757 (Oct.) 1932.

96 Combes, F. C. Pityriasis Rosea. Report of a Case with Lesions of the Palms and Soles, *Brit. J. Dermat.* 44:586, 1932.

itchy lesions resembling syphilids, on the palms and soles Haldin-Davis' ⁹⁷ patient also had lesions on the palms similar to syphilids, but the soles were clear and the Wassermann reaction of the blood was negative Weber's and Rattner's ⁹⁸ patient had typical pityriasis rosea on the trunk and lesions on the palms and soles which resembled those of vesicular ringworm but in which no fungi were found Milian's and Perrin's ⁹⁹ patient had dyshidrotic vesicles on the hands and the sides of the fingers, and Milian's ¹⁰⁰ patient had dyshidrotic bullae on the same areas Kern ⁹² stated that he had "often seen typical pityriasis rosea on the trunk associated with a dyshidrotic type of eruption on the hands and feet" Three of our patients had lesions on the feet and 1, on the hands, but none of them had lesions on both the hands and the feet

XIX LESIONS ON THE MUCOUS MEMBRANES

Guequiere ¹⁸⁸ presented a boy with typical pityriasis rosea on the trunk and a superficial eroded lesion on the right buccal mucosa In the discussion of this case he stated that he had found oral lesions in 3 of 8 patients with pityriasis rosea seen in the previous week and a half He also presented a girl ¹⁸⁹ with a painless annular lesion which had a red border and a slightly depressed, somewhat scaly center on the right buccal mucosa and which resembled the typical lesions of pityriasis rosea on her skin In the discussion of this case the diagnosis of the spot in the mouth was disputed Wile ¹⁰⁰ described a case in which first bullae appeared on the oral, nasal and vaginal mucosa and later typical lesions developed Hazen ⁴⁰ reported a case in which there were lesions on the mucous membranes, and Rosen ⁹⁴ saw a patient with lesions on the tongue Thomson and Cumings ²² found no lesions on the mucous membranes of 18 patients We saw no patients with lesions on the mucous membranes

XX INCIDENCE OF HERALD PLAQUE

The reports of various authors vary greatly regarding the incidence of the herald plaque MacLeod ³ and Heath ³ stated that it is usually present, while Ullmann ¹⁴ considered it rare Whitfield ³ stated the

97 Haldin-Davis, H Pityriasis Rosea with Lesions on Palms, *Brit J Dermat* 45 71, 1933

98 Weber, L F, and Rattner, H Clinical Variants of Familiar Diseases of the Skin Phenolphthalein Eruption, Pityriasis Rosea, Lichen Planus, Parapsoriasis, *Arch Dermat & Syph* 28 190 (Aug) 1933

99 Milian, G Pityriasis rosé à plaque initiale anormale et géante et accompagnée de dysidrose, *Rev franç de dermat et de veneréol* 12 81, 1936

100 In discussion on Shaffer, L W A Case for Diagnosis (Pityriasis Rosea?), *Arch Dermat & Syph* 25 766 (April) 1932

belief that the history of a herald patch is suggested to the patient and that it is really not as frequent as is usually thought. Pernet³ considered the herald patch an important diagnostic feature of the disease. It appeared in 12 per cent of Towle's^{16a} cases, 27 per cent of Owen's,²¹ 27 per cent of Weiss, Lane and Showman's,¹⁵ 50 per cent of Szaboky's,¹⁹ 54 per cent of Montgomery's²⁵ and 94 per cent of Highman and Rulison's.¹⁷ Thomson and Cummings²² observed the herald patch in 15 (83 per cent) of 18 cases, but Weiss,^{52b} in only 2 (14 per cent) of 14 and Little,⁴ in only 19 (11 per cent) of 174. A herald patch was noted in 90 (51.72 per cent) of 174 of our cases.

XXI THE INTERVAL BETWEEN THE APPEARANCE OF THE HERALD SPOT AND THAT OF THE GENERALIZED ERUPTION

The interval between the appearance of the herald spot and that of the generalized eruption, which Weiss, Lane and Showman¹⁵ termed "the secondary incubation period," was four days or less in 18 (40 per cent) of their 45 cases. The longest period was forty-seven days. Finnerud¹⁰¹ stated that in about 75 per cent of patients the herald spot appears four to ten days before the generalized eruption. Brocq^{65b} found this interval to be four to fifteen days, Adamson,¹¹ ten days, and Pernet,³ about one week. Little⁴ discovered no apparent incubation period in more than half his cases. The incubation period was from two to fourteen days in his other cases, one week in Finnerud's¹⁰¹ and in Reuter's¹⁰² case, two weeks and nine days respectively in Shellow's¹⁰³ 2 cases, three weeks in Gross's²⁹ case and one month in Kogoj and Farkas',⁷ five weeks in 1 of Thomson and Cummings' ²² cases, six weeks in Mongeard's²⁰ case and two months in Hallopeau's,^{44c} four to five months in Greenhouse and Cornell's¹⁰⁴ and six months in Schiller's.^{31b} The shortest interval reported in the literature was in Friedman's⁸⁵ case, in which the herald spot on the chin was followed in three hours by lesions on the face and four hours after this by an eruption on the neck, chest and abdomen. In 77 of our cases the generalized eruption appeared on an average of one and a half weeks after the herald patch was first seen. The shortest interval was one day, and the longest eight weeks.

101 Finnerud, C. W. Pityriasis Rosea, *M. Clin. North America* **13**:457, 1929.

102 Reuter, M. J. Thrombophlebitis and Pityriasis Rosea. *Arch. Dermat. & Syph.* **35**:1137 (June) 1937.

103 Shellow, H. Unusual Location of Herald Plaque of Pityriasis Rosea. *Arch. Dermat. & Syph.* **32**:106 (July) 1935.

104 Greenhouse, C., and Cornell, V. H. Pityriasis Rosea. Report of Case Showing a Gigantic Herald Plaque with Unusual Manifestations, *Arch. Dermat. & Syph.* **28**:823 (Dec.) 1933.

XXII LOCATION OF THE HERALD PLAQUE

The herald plaque is usually located on the trunk, but several reports of unusual sites are recorded in the literature. Both Guequierre^{38a} and Knowles³⁵ have stated that in the last few years they have observed several cases in which the herald plaque was in an unusual site, and Guequierre saw 1 patient with the herald plaque on the dorsum of the foot. The site of the herald plaque in eighty-six of Weiss', Lane's and Showman's¹⁵ cases was the anterior wall of the chest in 31, the arms in 12, the forearms in 10, the thighs in 10, the axillas in 5, the back in 4, the face in 4, the scapulas in 3, the buttocks in 3, the legs in 3 and the groin in 1. Szaboky¹⁰ found the herald plaque under the left clavicle in 77 per cent of his cases, under the right clavicle in 11 per cent, on the sacrum in 6 per cent and on one thigh in 6 per cent. In Maplestone's and Dey's¹⁰⁵ 19 cases the site of the herald plaque was an arm in 7, the abdomen in 5, the chest in 3, the back in 2, a thigh in 1 and the dorsum of the wrist in 1. Montgomery and Culver,⁹⁰ Schiller,^{31b} Hissard,¹² Ochs,¹² Eller,¹² Friedman,⁸⁵ Oulmann¹² and Fox^{32b} have reported cases in which the herald plaque was on the face. In Brocq's¹⁰⁶ case the herald plaque appeared around a gunshot wound on the thigh. Lord⁵³ cited a case in which the herald plaque was at the site of a vaccination. In Engman's and Kile's¹⁰⁷ patient, who had three attacks of pityriasis rosea, the herald plaque was twice on the left side of the neck. In Klauder's³⁷ case of recurrent pityriasis rosea, in the first attack the herald plaque was on the right hip and in the second it was back of the left knee. In Cabot's¹⁰⁸ case the herald plaque was on the right calf. Shellow¹⁰³ reported 2 cases and Montgomery and Culver,⁹⁰ 1 case in which the herald plaque was located on the glans penis. In 72 of our cases the herald patch was on the trunk in 37, an extremity in 24, the neck in 9 and the face in 2. In 1 the herald patch was on a palm, and in another, on the dorsum of one foot. We noted in many cases that the generalized eruption first appeared on an area far removed from the site of the herald patch, and in some instances secondary lesions never developed in this area. From these observations it can be assumed that the secondary lesions are not a direct extension from the herald plaque.

105 Maplestone, P. A., and Dey, N. C. *The Treatment of Pityriasis Rosea*, *Indian M. Gaz.* **72** 135, 1937.

106 Cited by Montgomery and Culver⁹⁰

107 Engman, M. F., Jr., and Kile, R. L. *Three Definite Attacks of Pityriasis Rosea in the Same Person*, *Arch. Dermat. & Syph.* **34** 272 (Aug.) 1936.

108 A Macular Rash with Slight Adenopathy, Cabot Case 15182, *New England J. Med.* **200** 941, 1929.

XXIII MULTIPLE HERALD PLAQUES

Maplestone and Dey¹⁰⁵ reported on 3 patients with multiple herald plaques. One patient had one on an arm and one on the chest, and in 2 patients two herald plaques appeared at the same time on the abdomen. Schiller's^{31b} patient had three typical herald spots simultaneously. One in the bend of the left elbow and two on the abdomen. In a discussion of this case Wile¹⁰⁹ stated that this was the first time that he had seen multiple herald spots. Veiel,⁹⁹ however, observed that in several hundred cases a double or triple focus (herald plaque) was frequent. Multiple herald plaques were found in 4 (5.5 per cent) of our cases. One patient had three herald spots on a forearm, 1, a herald spot on an arm and on a leg, 1, two herald spots on the right thigh, and 1, two on the back.

XXIV GIANT HERALD PLAQUE

Allen's^{110a} patient had a gigantic herald plaque covering half the chest wall, and Greenhouse and Cornell¹⁰⁴ reported on a patient with a giant initial plaque on the right scapular region which was sharply outlined, the size of a small palm and composed of red raised scaly concentric rings, with areas of clearing between the rings. Milian⁹⁹ reported a case in which an annular giant herald plaque extended all around the neck like a napkin. In Montgomery's and Culver's⁹⁰ patient the herald plaque was a large ring on the right cheek, and in Jadasohn's¹² patient it was the size of a child's head. None of our patients had a herald plaque large enough to be termed "giant."

XXV ITCHING

In the 380 cases of Weiss, Lane and Showman¹⁵ 102 patients (26.8 per cent) had itching. This was severe in 48 patients and moderate in 54. The authors considered itching a feature of the disease. MacLeod³ and Highman and Rulison¹⁷ also observed that severe itching was common, but Little⁴ stated the belief that it is rare. Montgomery¹² found this symptom in only 6 (15.8 per cent) of 38 cases, while in most of Savill's³ it was severe. Five (27.7 per cent) of Thomson's and Cummings'²² 18 patients complained of itching and 1 had actual excoriations. MacLeod³ expressed the opinion that itching is most frequent in toxic and neurotic patients, and Sutton⁵⁵ stated that it is associated with sweating. In our study 130 (72.2 per cent) of 180 of the patients complained of itching. This was slight in 30, moderate in 37 and severe in 63. It is interesting that excoriations were never seen even in the most severely itchy eruptions.

109 In discussion on Schiller³¹

110 In discussion on Fordyce⁵⁸

XXVI PIGMENTARY CHANGES FOLLOWING PITIRIASIS ROSEA

Stillians and Benedek¹⁰ presented the case of a Negress who had leukoderma for over sixteen months on the sites of former lesions of pityriasis rosea. Mitchell¹¹¹ said that he had seen the same condition which had been called "pityriasis alba," on the tanned body of a white man, and he saw another white man with pigmentation following the disease. Runtová¹¹² reported 3 cases in which macular hyperpigmentation followed the involution of the lesions of pityriasis rosea. This occurrence has also been reported by Duhning,⁴⁰ Jameson,⁴⁰ Whitfield³ and Little.¹ On their last visit several of our patients showed some pigmentation on the sites of former lesions but we do not know how long this persisted.

XXVII COMPLICATIONS

From our review of the literature and our own experience we can agree with Reuter's¹⁰² statement, "Complications and sequelae of pityriasis rosea are practically unknown." The only report of a complication of this disease which we could find was that of Reuter's patient who four weeks after the appearance of a herald spot on the left forearm had a thrombophlebitis of the same arm, for which no other cause could be found. There was diffuse edema of the entire arm from the dorsum of the hand to the shoulder, the skin of the arm was reddish brown, and the veins were thick and tender. This condition persisted for some time after the rash had disappeared.

XXVIII RECURRENCES

Butterworth³⁰ stated the belief that because the disease is uncommon the apparent immunity to pityriasis rosea may be based solely on the laws of chance. Stelwagon²⁰ stated, "According to Thibierge the disease does not recur, but this, I believe, does occasionally take place." Hazen⁵¹ stated, "The disease rarely recurs" and Pusey¹¹³ wrote, "Recurrence of the disease is rare, but occasionally happens." Ormsby²¹ commented, "Recurrences are rare, though we have noted several such instances. Towle and others have reported recurrent cases." After reading Towle's¹⁰⁶ report, we believe that his case should not be considered as one of a recurrence since the first eruption was not definitely diagnosed as pityriasis rosea. Second attacks have been

111 In discussion on Stillians and Benedek³⁰

112 Runtová, M. Macular Hyperpigmentation Following Pityriasis Rosea, *Ceska dermat* 15 193, 1934

113 Pusey, W. A. *The Principles and Practice of Dermatology*, New York, D Appleton and Company, 1925

reported by Sayer,¹¹⁴ Edelston,⁵³ Churchill,⁵³ McCaw,⁵³ Gray,¹⁰⁰ Dwyer,⁴⁵ Whitfield,³ Razen,²⁵ Robinson,¹¹⁵ Gourvitch,⁴⁶ Feldman,¹¹⁶ Montgomery and Culver,⁹⁰ Glaubeisohn,⁸ Shellow¹⁰⁷ and Kurtz and Davis⁵⁶ Kogoj and Farkas⁷ saw no recurrences in their series of cases, and Adamson,¹¹ Dore³ and Pernet³ stated that they had never seen a recurrence Thomson and Cumings²² in a large series of cases saw only one recurrence Klauder⁷⁰ reported a recurrence of pityriasis rosea and stated that this was only the third one he had ever seen Allen⁴⁰ had a patient with seven recurrences and another with three attacks, each of which occurred after a severe gastrointestinal upset from stopping the use of alcohol Schamberg^{33b} mentioned a physician who had pityriasis rosea three years in succession, and Zeisler⁴⁸ himself twice had the disease Sherwell's¹¹⁷ patient had pityriasis rosea during two successive pregnancies Weiss, Lane and Showman¹⁵ in 380 cases of the disease observed five recurrences The second attack appeared six months, eight months, one year, eighteen months and five years after the first They also saw 2 patients whose second eruption occurred twenty and twenty-five years later Sayer¹¹⁴ expressed the opinion that Weiss's, Lane's and Showman's¹⁵ cases in which there was only six months and 8 months between attacks were probably recrudescences and not true recurrences He reported 2 cases of true recurrences in which the second attack occurred four years and over two years, respectively, after the first He stressed the need of distinguishing between a second attack and a flare-up of the original eruption and suggested setting a minimum of one year's time as the limit between an attack and a true recurrence He said that the strong immunity developed prevents in a great majority of patients a recurrence of the disease Engman and Kile¹⁰⁷ reported three authenticated attacks of pityriasis rosea in the same person The intervals between attacks were four years and nine years There were two recurrences in our series One patient had a typical generalized pityriasis rosea which completely disappeared two weeks after she received 5 cc of immune serum Her second attack started four months later with a herald patch on the neck which was followed in two weeks by typical secondary lesions limited to the neck and the lower part of the face Histologic examination of one of these

114 Sayer, A Recurrences of Pityriasis Rosea Report of Two Cases, *Brit J Dermat* 46:181, 1934

115 Robinson, S S Recurrent Pityriasis Rosea Report of Two Cases, *Urol & Cutan Rev* 41:111, 1937

116 Feldman, S Pityriasis Rosea (Second Attack), *Arch Dermat & Syph* 24:898 (Nov) 1931

117 Sherwell S Pityriasis Rosea, *J Cutan Dis* 11:495 1893, in discussion on Fordyce "

lesions showed the picture of pityriasis rosea. The second patient had a herald patch and a typical generalized eruption five years after she had had a similar eruption which was diagnosed pityriasis rosea.

XXIX PITYRIASIS ROSEA IN CHILDREN

Pernet³ found pityriasis rosea more frequent in children than in adults. The youngest patient reported in the literature was one of Crocker's,⁶ aged 7 months. One third of his patients were children. Weiss, Lane and Showman¹¹ reported that 14.2 per cent of their patients were under 10 years of age and 1 was only 8 months old. Leiner¹¹⁸ reported pityriasis rosea in a child at the age of 21 months, Savill's³ patient was 11 months old, Little's,⁴ 18 months, 1 of Thomson's and Cumings',²² 21 months, and Adamson's,¹¹ 2 years. Lord's⁵³ son, aged 3, and Haas'⁵⁴ baby had typical pityriasis rosea. Finnerud's¹⁰¹ patient was 5, and Saad's¹¹⁹ 10. Kogoj's and Farkas'⁷ youngest patient was 9 years old. Of 153 of our patients 3.27 per cent were less than 10 years old and 22.22 per cent from 10 to 20. Our youngest patient was 5.

XXX COEXISTENCE OF PITYRIASIS ROSEA AND SYPHILIS

Benedek⁹¹ commented on the frequent occurrence of pityriasis rosea in persons with syphilis. Thomson and Cumings²² quoted Wise as stating that pityriasis rosea is more common in patients who have had syphilis and especially in those receiving arsenical therapy. Two of Kogoj's and Farkas'⁷ 46 patients with pityriasis rosea had syphilis. In our series pityriasis rosea developed in 2 patients with syphilis while they were receiving specific therapy and in another who had latent syphilis and a strongly positive Wassermann reaction of the blood.

XXXI TREATMENT

Little⁴ stated that the course of pityriasis rosea is so variable that it is difficult to evaluate the effects of treatment, and he is not convinced that any internal or external treatment shortens the duration. Montgomery and Culver⁹⁰ observed that symptoms were relieved and the course shortened by the treatment advocated by Jamieson of Edinburgh, which consists of hot potassium permanganate baths followed by the application of a 2 per cent salicylic acid ointment and talcum powder. Savill³ saw patients with a severe form of the disease recover in two

118 Leiner, C. Ein 1½ Jahre altes Kind mit Pityriasis rosea, *Mitt. d. Gesellsch. f. inn. Med. u. Kinderh.* 20: 25, 1921.

119 Saad, M. V. Epithelioma sur lupus tuberculeux et pityriasis rose de Gibert chez un enfant de 10 ans, *Bull. Soc. franç. de dermat. et syph.* 39: 552, 1932.

weeks after taking the baths once or twice a day at first and later applying a mild mercurial ointment. Whitfield³ and Bolam³ have observed that the duration is shortened by the use of a tar lotion but that the eruption and itching are made worse by sulfur salves. Pernet³ obtained good results with the use of salicin. Gougerot⁶¹ treated 12 patients with daily sponge baths, using 2 per cent eosin in 80 per cent alcohol. Herald plaques treated early did not enlarge, and the other lesions disappeared in fifteen to twenty days, while the lesions of pityriasis rosea treated with other methods lasted six to eight weeks. He obtained equally good results with a 6 per cent alcoholic solution of oil of bergamot. Leiner¹²⁰ used injections of milk in the treatment of the disease in children. Desquamation began four to five days after the injection, and involution of the rash began after one week.

Stillians and Benedek³⁰ gave a patient an intradermal injection of 0.1 cc of Benedek's vaccine.^{120a} The itching disappeared in one day and most of the rash in five days. Three days after a second injection the skin was entirely clear. Benedek also used this vaccine on a nurse with a severely itchy, extensive eruption of three days' duration. The itching disappeared and the rash became dull red and desquamated after the first injection, and the eruption entirely disappeared after the second. Gourvitch⁴⁶ treated 26 patients with intravenous injections of sodium thiosulfate, sodium salicylate by mouth and two to three subcutaneous injections of 0.5 to 1 cc of a streptococcus vaccine. In all the patients the course was shortened, the eruption never lasting more than twelve to eighteen days. Barradah¹²¹ reported on 2 patients treated with intravenous injections of streptococcus vaccine. One had received three injections in nine days, and his eruption disappeared four days after the last injection, and the other had had three injections and was well in 13 days. Maplestone and Dey¹⁰⁵ obtained from a patient a recent spot of pityriasis rosea with which they made a saline solution and of which 0.1 cc, increased by 0.1 to 0.5 cc, was injected every three to four days. Twenty-eight patients were cured in six to twenty (average, eleven and one-fifth) days with three to six injections.

Ormsby²¹ stated "Phototherapy often causes the lesions to undergo involution rapidly. . . . Mild exposures to roentgen rays are followed by prompt cessation of subjective sensations and by more rapid involu-

120 Leiner, C. Zur Behandlung der Pityriasis rosea im Kindesalter mit Milchinjektionen, *Wien med Wchnschr* 71:1801, 1921.

120a This was made from an 8 per cent dextrose agar culture of *Schizosaccharomyces hominis*.

121 Barradah, M. K. The Cure of Pityriasis Rosea—New Treatment, *J Egyptian M A* 18:766 1935.

tion of the lesions" MacKee¹²² observed, "Ultra-violet irradiation has been more efficacious than has x-ray treatment" but considered the possibility of the latter's being of value in severe and persistent conditions. He cited Luner's case in which the eruption disappeared in one week after a single exposure of 75 r of unfiltered roentgen rays. Allen¹²³ treated 3 patients with pityriasis rosea with roentgen rays and declared that in each case the eruption disappeared more rapidly than it would have with the use of regular topical remedies. In Blaschko's¹²⁴ case the eruption disappeared in two weeks with roentgen therapy. Hazen¹²⁵ admitted that roentgen rays cause a rapid disappearance of the lesions, but he considered it unwise to use general irradiation unless necessary. King and Hamilton¹²¹ found that pityriasis rosea disappeared more rapidly after 150 to 225 r of roentgen rays than after any other treatment. In some cases they irradiated half of the body and found that the eruption on the treated half disappeared an average two weeks sooner than that on the untreated. Markson and Miller¹²⁵ expressed the opinion that two to three subfractional weekly doses of roentgen rays shorten the course of pityriasis rosea. Lord¹²¹ applied half of an erythema dose of unfiltered roentgen rays to a herald plaque on his wife's skin. In seventeen days the spot completely disappeared, without leaving a trace, and there was no generalized eruption. Hazen¹²¹ reported his results with ultraviolet irradiation: 7 patients were cured in four to five days with one treatment, 3, in eight to ten days with two treatments, 9, in twelve to fourteen days with two to three treatments, 4 in twenty days with four to five treatments, 3, in twenty-eight days with six to seven treatments, and 1, in six weeks with eight treatments. He asserted that slight erythema doses are necessary to produce results.

In an extensive review of the literature we found no mention of the therapeutic use of immune serum in pityriasis rosea.

AUTHORS' SERIES

The rarity of recurrence of pityriasis rosea suggested to us that the serum of patients who had had this disease might possess immune properties. Although there have been a great number of studies on pityriasis rosea, its cause is still unknown. We thought that if it could

122 MacKee, G. M. *X-Rays and Radium in the Treatment of the Diseases of the Skin*, Philadelphia, Lea & Febiger, 1938, p. 735.

123 Cited by MacKee¹²².

124 Blaschko, A. *Zur Röntgenbehandlung der Hautkrankheiten*, Verhandl. d. Berl. med. Gesellsch. (1908) (pt. 2) 39:39, 1909, abstracted, Arch. Roentgen Ray 14:129, 1909.

125 Markson, S. M., and Miller, H. L. *Pityriasis Rosea*, Wisconsin M. J. 35:875, 1936.

he demonstrated that convalescent pityriasis rosea serum has immune properties, an important step would be made toward finding the cause of this disease

We were able to follow the results of treatment in only 114 of our 219 patients. They were divided into three groups. Fifty had received generalized ultraviolet irradiation with a quartz mercury vapor glow lamp, 38, convalescent pityriasis rosea serum, and 26 controls, only soothing applications. When indicated, patients in all three groups had been treated symptomatically, as we found that if no attempts were made to allay the troublesome symptoms the patients would not return. The treatment consisted of the application of antipruritic lotions and creams and a bland oil or cream for extreme dryness, starch baths and the administration of phenobarbital when itching caused insomnia.

The chief factor which determined the grouping of the patients was the supply of serum, which was always relatively scarce, owing to the difficulty of persuading patients to return to the clinic after they were well, in order for us to obtain their blood for use in other patients. It was also usually impossible to obtain more than 20 to 35 cc. from any one donor. Patients who on their first visit had had a generalized eruption for one week or less were given serum whenever it was available. Those whose eruption had been present longer received serum only when there was an excess supply. We preferred treating the disease in its early stages in order to eliminate the factor of spontaneous involution. The remaining patients were either treated with ultraviolet irradiation from a quartz mercury vapor glow lamp or used as controls. Patients with severe eruptions were treated with ultraviolet rays because we thought that they might not return unless given intensive treatment.

Fifty patients were given one to eight treatments with ultraviolet rays from a quartz mercury vapor glow lamp at intervals of one to three times a week. For the first treatment we gave a dose which we expected would produce a mild erythema. From the effect of this treatment the erythema dose for each person was determined and was given thereafter. Most of the exposures were followed by desquamation, which frequently caused the itching to become worse because of the associated dryness. We were surprised to note that in our series the ultraviolet irradiation did not shorten the total duration. This form of therapy, however, had an immediate beneficial effect, as after even one or two treatments the patches became much drier and paler and seemed to peel off. We found that ultraviolet rays from a quartz mercury vapor glow lamp were more effective than other forms of radiation. The lesions desquamated profusely, even when there was no scaling of the surrounding normal skin. This often gave the patches the appearance of having been scraped off with a knife.

Thirty-eight patients received serum. Blood was obtained from patients from all three groups on the day on which they were discharged as cured. The clot was allowed to retract and the serum was drawn off and placed in the ice box until needed. In every case a Wassermann test was performed at the time the blood to be used for serum was drawn. When the supply permitted, 5 cc was injected intramuscularly once, and occasionally twice, a week. Only 1 patient was given more than three injections. The patients who received serum soon became more comfortable, many stated emphatically that the itching ceased shortly after one injection. This subjective improvement may have been suggested by the method of treatment.

We did not know to what, if any, extent the immune properties of the serum would deteriorate on standing in the ice box, but we found that the effectiveness of the serum, as measured by the duration of the eruption on the patient to whom it was administered, was not related to the length of time which elapsed between the drawing and the use of the serum. There were no serums which proved especially potent, and the effect of the same serum varied in different recipients. We frequently discovered that after the same serum was given to 2 patients, the eruption disappeared rapidly in 1 and slowly in the other. As can be seen in table 1, "second generation serum" (serum from patients who themselves had received serum) was no more effective than that obtained from patients in the other two groups. Neither the duration of the eruption before treatment nor the duration, type or severity of the donor's eruption appeared to affect the results.

Patients in the control group received only mild antipruritic topical remedies. In some patients it became increasingly difficult, the longer the duration of the eruption, to maintain their confidence. We therefore found it necessary to vary the applications from time to time.

We calculated the duration of the illness as the interval between the onset of the generalized eruption and the date of cure. The data on the time of appearance of the herald patch was too unreliable to use. The criteria for cure were the absence of new lesions, the fading, flattening and softening of the old lesions, and the disappearance of itching.

The duration of the eruption, both from the onset to the cure and from the first treatment to the cure, was slightly shorter in the group treated with serum (three and nine-tenths weeks and two and one-half weeks), and slightly longer in a group treated with ultraviolet rays from a quartz mercury vapor glow lamp (five and three-tenths weeks and three and one-tenth weeks), than in the controls (four and seven-tenths weeks and three and one-fifth weeks). We do not claim that we have demonstrated immune properties in the convalescent serum, but we do believe that it is unjustifiable to conclude that the serum has no value until it has been used in a greater number of patients, in larger doses, at shorter

intervals and in subcutaneous and intracutaneous injections. Our equivocal results may have been due to insufficient quantities of serum, too few or infrequent injections or an inadequate method of adminis-

TABLE 1—*Analysis of Factors in Group Treated with Serum**

| Patient's Number | Duration in Weeks from Beginning of Treatment Until Cure | Total Duration of Eruption in Weeks | Duration in Weeks of Eruption at Time Treatment Was Begun | Origin of Serum Administered (Number is That of Donor) | "Second Generation Serum" (Serum from Patients Who Had Been Given Serum) | Interval Between Time Serum Was Obtained and Administered in Weeks |
|------------------|--|-------------------------------------|---|--|--|--|
| 11 | 0.6 | 2.6 | 2.0 | 4 | | 1.1 |
| 36 | 0.6 | 1.0 | 0.4 | 27 | 27 | 1.1 |
| 20 | 1.0 | 6.0 | 3.0 | 12 and 7 mixed | | 4.4, 2.4 |
| 85 | 1.4 | 2.4 | 1.0 | 80 | | 1.3 |
| 10 | 1.5 | 3.5 | 2.0 | 2, 4 | | 0.4, 1.0 |
| 20 | 1.5 | 5.5 | 4.0 | 8 | | 5.4 |
| 171 | 1.5 | 3.0 | 1.5 | 160 | | 0.7 |
| 50 | 1.7 | 2.7 | 1.0 | 46 | 48 | 1.5 |
| 24 | 2.0 | 7.0 | 1.0 | 10, 11, 15 mixed | 10, 11 | 6.3, 2.4, 4.3 |
| 43 | 2.0 | 3.0 | 1.0 | 42 | | 0.3 |
| 76 | 2.0 | 3.0 | 1.0 | 66 | | 3.0 |
| 104 | 2.0 | 3.0 | 1.0 | 93, 88, 91 | | 0.7, 1.0, 0.8 |
| 107 | 2.0 | 3.4 | 1.4 | 87, 91 | | 0.8, 1.4 |
| 121 | 2.0 | 3.0 | 1.0 | 114 | | 0.7 |
| 126 | 2.0 | 7.0 | 5.0 | ? | | ? |
| 127 | 2.0 | 2.3 | 0.3 | 118 | | 5.3 |
| 154 | 2.0 | 3.0 | 1.0 | 126 | 120 | 2.0 |
| 162 | 2.0 | 3.0 | 1.0 | 141 | | 1.4 |
| 27 | 2.2 | 2.6 | 0.4 | K,† K,† 25, 26 | | 0.0, 0.0, 0.7, 5.8 |
| 133 | 2.3 | 4.3 | 2.0 | 127 | 127 | 3.4 |
| 129 | 2.4 | 3.0 | 0.6 | 125 | | 4.0 |
| 115 | 2.4 | 2.5 | 0.1 | 94, 103, 109 | | 8.4, 4.7, 4.4 |
| 130 | 2.5 | 7.3 | 0.8 | 122 | | 9.3 |
| 158 | 2.5 | 7.7 | 1.2 | 121 | | ? |
| 110 | 2.6 | 3.0 | 0.4 | 100, 100, 93 | 100 | 1.4, 2.3, 4.2 |
| 21 | 3.0 | 7.6 | 0.6 | 11 | 11 | 4.5 |
| 22 | 3.0 | 7.0 | 2.0 | 14, 11 | 11 | 5.0 |
| 39 | 3.0 | 4.0 | 1.0 | 28, 29 | | 4.4, 1.8 |
| 50 | 3.0 | 4.0 | 1.0 | 44 | | 12.3 |
| 100 | 3.0 | 4.4 | 1.4 | 92, 90 | 90 | 1.3, 2.1 |
| 117 | 3.0 | 4.4 | 1.4 | 109, 107, 95 | 107 | 4.4, 7.7, 2.0 |
| 58 | 3.6 | 4.0 | 0.4 | Mixed | | ? |
| 69 | 4.0 | 5.5 | 1.5 | ? | | ? |
| 123 | 4.0 | 5.5 | 1.5 | 117 | 117 | 2.5 |
| 164 | 4.0 | 6.4 | 2.4 | 141, 153 | | 2.0, 2.3 |
| 71 | 4.3 | 5.0 | 0.7 | 59 | | 1.0 |
| 90 | 5.0 | 6.0 | 1.0 | 82 | | 1.0 |
| 72 | 7.0 | 8.0 | 1.0 | 54, 67, 63 | | 2.0, 0.7, 0.7 |

Summary (Average in 19 Patients)

| | Duration in Weeks from Beginning of Treatment Until Cured | Total Duration of Eruption in Weeks | Duration in Weeks of Eruption at Time Treatment Was Begun | Interval Between Time Serum Was Obtained and Administered in Weeks |
|---|---|-------------------------------------|---|--|
| Patients with shortest duration | 1.7 | 3.4 | 1.7 | 2.2 |
| Patients with longest duration | 3.4 | 4.5 | 1.1 | 3.3 |
| Patients treated with "second generation serum" | 2.5 | 3.6 | 1.2 | 3.2 |

* Patients who received serum are listed in the order of duration of the eruption from the time serum was first injected until they were well.

† Whole blood obtained from a private patient.

tration. The effect of this serum should also be compared with that of ordinary whole blood and serum. We plan to continue this work and to investigate several other features of pityriasis rosea.

TABLE 2—*Effect of Treatment with Ultraviolet Rays from a Quartz Mercury Vapor Glow Lamp and Convalescent Serum on the Duration of Pityriasis Rosca*

| Cold Quartz Ultraviolet Rays | | | Control | | | Convalescent Serum | | |
|----------------------------------|-------------------------------------|------------------------------------|------------------------------|-------------------------------------|------------------------------------|--------------------|-------------------------------------|------------------------------------|
| Patient's Number | Total Duration of Eruption in Weeks | Duration After Treatment Was Begun | Patient's Number | Total Duration of Eruption in Weeks | Duration After Treatment Was Begun | Patient's Number | Total Duration of Eruption in Weeks | Duration After Treatment Was Begun |
| 2 | 6.0 | 4.0 | 12 | 3.5 | 0.6 | 10 | 3.5 | 1.5 |
| 3 | 3.0 | 1.0 | 14 | 6.0 | 2.0 | 11 | 2.6 | 0.5 |
| 4 | 3.0 | 1.0 | 28 | 1.7 | 1.0 | 20 | 6.0 | 1.0 |
| 7 | 4.0 | 3.0 | 35 | 1.4 | 1.0 | 21 | 3.6 | 3.0 |
| 8 | 4.0 | 2.0 | 42 | 6.0 | 5.0 | 22 | 5.0 | 3.0 |
| 15 | 5.0 | 4.0 | 54 | 5.3 | 3.0 | 24 | 3.0 | 2.0 |
| 17 | 3.5 | 1.0 | 59 | 5.4 | 3.4 | 25 | 5.5 | 1.5 |
| 25 | 8.2 | 6.2 | 64 | 5.0 | 5.0 | 27 | 2.6 | 2.2 |
| 29 | 4.0 | 1.6 | 87 | 5.7 | 3.7 | 36 | 1.0 | 0.6 |
| 31 | 6.6 | 5.6 | 92 | 3.0 | 2.0 | 39 | 4.0 | 3.0 |
| 44 | 4.0 | 2.5 | 103 | 6.0 | 2.0 | 40 | 3.0 | 2.0 |
| 46 | 3.0 | 2.6 | 109 | 6.0 | 4.0 | 50 | 2.7 | 1.7 |
| 49 | 3.0 | 2.0 | 111 | 5.0 | 4.0 | 55 | 4.0 | 3.0 |
| 57 | 6.0 | 4.0 | 116 | 3.0 | 4.0 | 58 | 4.0 | 3.0 |
| 60 | 3.5 | 2.5 | 118 | 9.0 | 5.0 | 62 | 5.5 | 4.0 |
| 61 | 6.0 | 3.0 | 123 | 5.0 | 4.0 | 71† | 5.0 | 4.3 |
| 63 | 7.0 | 4.0 | 129 | 4.0 | 3.9 | 72 | 8.0 | 7.0 |
| 66 | 6.0 | 3.0 | 141 | 1.0 | 1.1 | 76 | 3.0 | 2.0 |
| 67 | 4.0 | 2.0 | 150 | 5.1 | 3.1 | 85 | 2.4 | 1.4 |
| 68 | 4.6 | 2.6 | 156 | 3.2 | 2.2 | 90† | 6.0 | 5.0 |
| 71* | 5.0 | 2.3 | 160 | 5.0 | 3.0 | 100 | 4.4 | 3.0 |
| 73 | 4.0 | 2.0 | 161 | 11.0 | 10.0 | 104 | 3.0 | 2.0 |
| 79 | 7.6 | 5.0 | 165 | 5.6 | 3.6 | 107 | 3.4 | 2.0 |
| 80 | 6.0 | 3.0 | 177 | 3.4 | 2.0 | 110 | 3.0 | 2.6 |
| 82 | 6.0 | 3.0 | 192 | 0.6 | 0.3 | 115 | 2.5 | 2.4 |
| 85 | 6.0 | 2.0 | 197 | 2.0 | 0.9 | 117 | 4.4 | 3.0 |
| 90* | 6.0 | 1.6 | | | | 121 | 3.0 | 2.0 |
| 91 | 5.0 | 3.0 | Total | Average | Average | 122 | 5.5 | 4.0 |
| 93 | 7.0 | 6.0 | Number | Duration | Duration | 126† | 7.0 | 2.0 |
| 94 | 5.2 | 4.7 | Patients | in Weeks | in Weeks | 127 | 2.3 | 2.0 |
| 95 | 4.7 | 1.7 | 26 | 4.7 | 3.2 | 129 | 3.0 | 2.4 |
| 96 | 4.0 | 2.5 | | | | 130 | 3.3 | 2.5 |
| 97 | 6.0 | 3.5 | | | | 132 | 4.3 | 2.3 |
| 114 | 7.0 | 3.0 | | | | 134 | 3.0 | 2.0 |
| 122 | 10.0 | 6.0 | | | | 138 | 2.7 | 2.5 |
| 124 | 4.0 | 1.4 | | | | 162 | 3.0 | 2.0 |
| 126* | 7.9 | 6.9 | | | | 164 | 6.4 | 4.0 |
| 144 | 4.3 | 3.2 | | | | 171 | 3.0 | 1.5 |
| 167 | 4.4 | 3.0 | | | | | | |
| 175 | 3.6 | 3.0 | | | | Total | Average | Average |
| 179 | 6.0 | 2.6 | | | | Number | Duration | Duration |
| 185 | 6.0 | 3.6 | | | | Patients | in Weeks | in Weeks |
| 186 | 12.1 | 3.1 | | | | 33 | 3.9 | 2.5 |
| 190 | 10.4 | 5.3 | | | | | | |
| 191 | 4.3 | 2.3 | | | | | | |
| 193 | 6.1 | 4.1 | | | | | | |
| 195 | 4.4 | 2.9 | | | | | | |
| 196 | 3.1 | 2.4 | | | | | | |
| 199 | 3.0 | 1.1 | | | | | | |
| 204 | 1.9 | 0.9 | | | | | | |
| Total | Average | Average | Summary | | | | | |
| Number Patients | Duration in Weeks | Duration in Weeks | Cold Quartz Ultraviolet Rays | | | | | |
| 50 | 5.3 | 3.1 | | | | | | |
| Number of cases | | | 50 | 25 | 35 | | | |
| Total duration, in weeks | | | 5.3 | 4.7 | 3.9 | | | |
| Duration from onset of treatment | | | 3.1 | 3.2 | 2.5 | | | |

* Also received serum

† Also received ultraviolet radiation.

ABSTRACT OF DISCUSSION

DR CARROLL S WRIGHT, Philadelphia I have been particularly interested in the question of lesions of the mucous membranes in connection with pityriasis rosea. Two and a half years ago Dr Guequierre, working in my clinic, showed me a lesion on the mucous membrane of a patient with pityriasis rosea. It was an oval lesion on the buccal mucosa on the right side and appeared slightly plaque-like, annular in contour and somewhat suggestive of the type of lesion that one sees on the skin. I suggested that he bring the patient to the meeting of the Philadelphia Dermatological Society, and the case has since been recorded in the transactions of that meeting (*ARCH DERMAT & SYPH* 33:262 [Aug] 1938). At this time Dr Guequierre began to pay particular attention to such lesions in patients with pityriasis rosea. I believe he has been able to find at least one such lesion in every 10 or 12 cases. There is nothing in the literature on the subject and practically no reference in any textbook except in George Clinton Anders' text on Diseases of the Skin (Philadelphia, W B Saunders Company). I feel that lesions on the mucous membrane can be easily overlooked. Sometimes one cannot find any, but that does not necessarily mean that there are none. It is strange that our experience should so distinctly disagree with that of Dr Niles. The lesion on the mucous membrane has usually disappeared at the same time that the lesions disappeared from the body in the cases that I have followed to the end of the disease.

DR JACOB HYAMS SWARTZ, Boston I want to report more than 1 case of pityriasis rosea in my own home. Two weeks ago Mrs Swartz became ill with pityriasis rosea, and one week later, the maid, and just before I left our child showed what might be a herald plaque. The three of them had a severe streptococcal infection of the throat about four weeks ago. I was the only one to escape the streptococcal infection, and so far I am the only one to escape the pityriasis rosea. It is interesting to note, moreover, that submaxillary adenitis preceded and accompanied the pityriasis rosea in the case of Mrs Swartz.

DR RICHARD S WEISS, St Louis In most of the statistical part of his work, Dr Niles has agreed with the observations in the study that Lane, Showman and I had made in 1926 (*ARCH DERMAT & SYPH* 15:304 [March] 1927). There is however, one point in which he differed, and I think correctly so, and that is that he found the herald patch in a much larger percentage of cases. Since 1926 my co-workers and I have been searching for the patch with greater care and have found it in a higher percentage of cases. His figure is 52 per cent, whereas ours was only 27 per cent.

He stated that we had reported itching as a feature of the disease. We did not quite make that statement. It was a feature of the disease in 26 per cent of the cases.

I was interested in his use of serum but cannot place much dependence on it from the standpoint of causation. Dr Niles is doubtless aware that this part of his work is incomplete because of lack of controls. It is uncertain whether or not he would have secured the same result by injecting a foreign protein that does not produce a very severe reaction, which could be used as a control to see whether or not the reduction in the duration of the disease is actual and not due to foreign protein reaction. I think too that he did not employ this serum with the expectation of curing pityriasis rosea, because all physicians know that the condition clears up no matter what one does. If the patients are given relief, in the course of one or two months at most by far the greater percentage get well. I assume that Dr Niles wanted to get on the track of some agent present perhaps in convalescent serum that might give a clue to the cause of the disease.

DR E WILLIAM ABRAMOWITZ, New York It is believed that strong topical agents should be avoided in the treatment of pityriasis rosea, because the skin

of patients with this condition is easily irritated. This statement is based on the frequent observation of sulfur dermatitis from the use of the commonplace sulfur ointments. My experience with the use of 30 per cent precipitated sulfur in petrolatum in the treatment of pityriasis rosea indicates that the cutaneous lesions disappear much earlier than usual. Moriz Oppenheim, of Vienna, stated that a strong sulfur ointment was the standard treatment for pityriasis rosea as far back as Neumann's time.

DR PAUL E. BECHET, New York. I have had such success with the quartz mercury vapor lamp in the treatment of pityriasis rosea that I was a little surprised at the indifferent results reported by Dr Niles. I should like to ask whether he has administered fairly severe erythema doses. My best results always followed a fairly severe reaction. Under these circumstances a cure usually followed two to four treatments.

DR FRED WISF, New York. Approximately 3 per cent of the patients I have examined in the past few years have had cervical and axillary adenopathy, an observation mentioned in connection with pityriasis rosea in most textbooks.

DR HENRY NILES, New York. In reply to Dr Wright, as I reported, we did not find any lesions on the mucous membranes. We thought at first that their apparent rarity was because they were not looked for, but we looked and still could not find them. We began examining the mouths of the patients with pityriasis rosea after we had started reviewing the literature and saw Dr Guequierre's report.

In respect to Dr Swartz's remarks, there are at least three or four reports in the literature on the relation of streptococcus infection to pityriasis rosea, and series are reported in which as high as 80 to 90 per cent of patients with this disease have given positive reactions to streptococcus vaccine, but only 15 per cent reacted to staphylococcus vaccine, and 95 per cent of the control cases gave a negative reaction to streptococcus vaccine. There are also reported cases of pityriasis rosea associated with proved streptococcus infection, such as bullous impetigo and erysipelas.

In answer to Dr Weiss's remark regarding controls, I know we had only 26 controls. It was difficult to keep patients as controls because they would not continue coming to the clinic unless something was done for them. That is the reason why we had more patients (50) treated by ultraviolet radiation, as we often ran short of serum and could not persuade them to come in and be just controls. We are going to treat a much larger series, and we may have some more conclusive results. As Dr Weiss mentioned, we did not do this work in an attempt to cure a self-limited disease, but to get some idea as to the causation.

In answer to Dr Bechet, I am more surprised at the failure of ultraviolet radiation in this disease than at anything else we found. My previous experience with this treatment had been the same as his. The only explanation is perhaps that our criteria for judging complete cure were too rigid—complete absence of itching, no new lesions and flattening, paling and loss of infiltration of the old lesions. Ultraviolet radiation, as a method of cure, is not of such great value under these rigid tests. We can obtain 75 to 80 per cent improvement with two or three such treatments, but not that last 20 to 25 per cent, so that we can say the patient is 100 per cent cured by the ultraviolet rays.

In regard to Dr Wise's question about adenitis, we looked for this in at least half our cases, but found it in very few. Dr Hazen has commented on the frequent involvement of the lymph nodes, particularly the cervical. Generalized adenopathy has also been described. I admit that our results with immune serum are inconclusive at present.

LESIONS OF THE ORAL CAVITY CAUSED BY PHYSICAL AND BY PHYSICOCHEMICAL FACTORS

EVERETT S LAIN, M D
OKLAHOMA CITY

The oral mucosa together with the epithelium of the tongue and teeth is closely related genetically, anatomically and sympathetically to the cutaneous covering of the human body. The mouth also constitutes the beginning of the alimentary canal, hence the primitive physician learned by experience the value of routine inspection of the lingual and oral mucosa, and from such examinations he attempted to diagnose many ailments of the internal organs. Physicians today have become fairly alert to localized infections and systemic disorders which may first appear or be reflected in the oral mucosa. Early dental teaching placed much emphasis on mechanical skill in dental reconstructions, but not until recent years have physicians and dentists fully appreciated the etiologic importance of allergic, physical or physicochemical factors in lesions of the mouth. This is my reason for presenting an investigation of the subject.

It is remarkable how well the structures of the mouth are able to withstand almost continuous injury. This is doubtless because the oral cavity is composed of resistant stratified epithelium capable of rapid restoration and continually lubricated with a copious flow of mucous and salivary secretion. The submucosa is abundantly supplied with small blood and lymph vessels.

EXAMINATION OF THE ORAL CAVITY

A satisfactory examination of the oral cavity consists of more than a glance at the protruded tongue or into the mouth without the aid of a diagnostic light. The physician must be able to observe and interpret certain abnormal findings and to differentiate between those which are obviously systemic and those which appear to be due to local causes. He should remove any detachable dentures and inspect every area of the mouth, especially the buccal surfaces, the inner surfaces of the lips, the gums and the soft and the hard palate and the tongue from tip to base, using a laryngeal mirror if necessary. If lesions are found, he

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should first look for any irregular, serrated, broken or decayed teeth or metallic or other dental restorative materials which might be primary or contributory causative factors

LESIONS DUE TO PHYSICAL OR PHYSICOCHEMICAL FACTORS

Lesions of the oral cavity due to physical or physicochemical factors may be classified as follows

1 Physical (traumatic) localized lesions, such as erosions, ulcers, papillomas, hematomas, fibromas, granulomas, verrucae and cysts and other lesions, such as leukoplakia and cancer, in which chronic irritation is generally accepted as a contributing or predisposing factor

2 Mechanophysical lesions due to abnormal or distorted development of the grinding teeth or unbalanced, maloccluded artificial dentures which may cause certain reflex symptoms of the tongue

3 Chemical lesions due to (a) thermochemical causes acute burns from hot liquids, cauterizing chemicals or tobacco and (b) allergic causes, reactions to certain dentifrices or toxic materials used in restorative dental work

4 Electrogalvanic discolorations of tissues or metals, erosions and ulcers caused by the difference of electropotentialities of the heterogeneous metals used in various types of dental reconstruction with the subsequent deposition of metals in the tissue

1 *Lesions Due to Physical (Traumatic Factors)* —Since the advent of instruction in dental hygiene in the public schools, with its emphasis on the use of the hard or stiff brush, I have observed erosions or ulcers occurring on the gingivae and on the margins of the tongue. These traumatic lesions are most often found on the floor of the mouth and are probably due to overzealous use of the unsterile toothbrush. In contrast with this industrious habit, physicians and dentists are often confronted with evidence of gross neglect of oral hygiene by the aged or the illiterate, such as carious, serrated, broken teeth, overhanging, rough crowns or bridges or ill-fitting artificial dentures.

Prinz and Greenbaum¹ have emphasized the fact that every artificial denture is at best a foreign body and a potential source of mechanical irritation through its interference with certain physiologic functions. A few weeks after the installation of dental plates, changes in the mouth may begin to take place of which the patient is unaware. In the average clinic, routine examination of the mouth will reveal many instances of progressive shrinkage of the gingival tissue and atrophy of the maxillary processes, leaving loose, noncoapting dentures which have become sources of chronic irritation. Lesions from such

1 Prinz, H, and Greenbaum, S. S. *Diseases of the Mouth and Their Treatment*, Philadelphia, Lea & Febiger, 1935, p. 213

a cause may become so large and painful as to interfere with mastication before the patient consults a dentist or a physician

Sutton,² Greenbaum and others have called attention to a certain type of granulomatous lesion occurring in the sulcus of the superior labial alveolar fold, which Sutton has named *granuloma fissuratum*. I have observed several such lesions both at the superior and the inferior labial fold. They are usually caused by trauma from a wing of ill-fitting dentures.

The tongue suffers equally with other structures of the oral cavity from accidental biting or from hot or chemically irritating fluids, and it may become inflamed and edematous after excessive use of tobacco and alcohol. It may undergo dorsal dekeratinization from rough or chemically irritating dentures. It often reflects the color of the denture and is spoken of as a bald or a varnished tongue. In such cases chemical examination of the blood or other laboratory analyses may become necessary to determine whether the cause is organic or local.

Convoluting Tongue, or Scrotal Tongue. This is a congenital and usually hereditary anomaly and may be unrecognized until persistent accumulations of food and debris in the furrows cause almost constant irritation. It then becomes a source of much physical discomfort and mental anxiety and requires intelligent hygienic treatment and reassuring advice from a physician or a dentist.

Serrated Tongue. During sleep or when the mouth is closed and the teeth are occluded the tongue fits snugly into the floor of the mouth between the wings of the mandibles. The margins of the tongue are drawn by suction firmly into the occlusal lines and other interspaces of the teeth. Should there be missing teeth, irregular, distorted teeth or malocclusion, the tongue after many months or years in such a periodically strained position may show indentations or projecting notched margins corresponding to the interspaces of the teeth. The labial or buccal mucosa may become molded by the same process into projecting or overlapping folds which are easily traumatized during mastication.

Hyperplasia of Circumvallate Papillae (Lingual Tonsils). Certain persons have a predisposition to hyperplasia of all lymphoid structures. A fairly common condition, second only to glossopyrosis as a cause of anxiety, is hyperplasia with a burning sensation of the circumvallate papillae, or lingual tonsils, distributed over the base and posterior margins of the tongue. Textbook descriptions of pathologic processes of the lingual tonsils are extremely brief, and discussions in the literature are rare. The great majority of the patients are hypersensitive women.

² Sutton R. L., Jr. (a) A Fissured Granulomatous Lesion of the Upper Labio-Alveolar Fold, *Arch Dermat & Syph* 26:425 (Sept.) 1932, (b) *Granuloma Fissuratum*, *ibid* 26:865 (Nov.) 1932.

or neurotic men, doubtless because, as was suggested by Miller,³ emotional stress is conducive to engorgement of the various plexuses at the base of the tongue. While the patient is usually conscious only of a single lesion on one side or on the dorsum of the tongue, this papillary enlargement is often bilateral. Many causes have been suggested. I agree with others that local irritation from certain foods and drinks, accumulation of debris and infection in the open crypts of the papillae constitute the cause in most cases. I am convinced that overanxiety and frequent examinations by both patient and physician are the principal contributing etiologic factors in more than 50 per cent of all such cases. It must not be forgotten that the lingual tonsils are common primary locations of cancer. In every case careful examination should be made, together with histologic examination if the latter is indicated.

Papillomas (Granulomas) Without histologic examination fibrous papillomas of the mouth are not easily differentiated from verrucae. Careful inspection reveals that fibromas usually arise from a portion of the buccal or lingual mucosa which has been drawn by suction into some abnormal dental interspace or dental reconstruction during sleep or when the mouth is closed. Such a tumor often becomes as large as an English pea before the patient's attention is drawn to it by biting or by some other injury.

Pyogenic granulomas often arise at the gingivodental junction although they may occur on the tongue or in any part of the buccal mucosa where a slight traumatic erosion and secondary pyogenic infection have occurred. They may be caused by piercing bristles of an unsterile toothbrush, or toothpicks or by neglect of dental hygiene which has permitted deposition of calcareous material on the periodontal structure below the gingival margins. Erroneous (histologic) reports of malignant disease are occasionally made unless there is also a clear roentgenogram of the tooth.

Verrucae Verrucae of the mouth are easily recognized, although their surfaces appear moist instead of dry like those of verrucae on the cutaneous surface. Approximately all forms of true verrucae may be due to the same virus and may differ only by reason of environment. They are infectious and autoinoculable in susceptible persons and may occur wherever superficial epithelial tissue is found. They may be present on the lips, the gingivae and the buccal mucosa, although the most frequent site is on the anterior margins or the dorsum of the tongue, a region corresponding to a point of irritation from an irregular, serrated tooth or rough dental reconstruction. Bloodgood and others have called attention to the fact that owing to constant irritation

3 Miller, M. V. The Lingual Tonsil, *Laryngoscope* 40 117 (Feb.) 1930

warts in the mouth may after a time undergo malignant degeneration and for that reason should always be removed

Cysts Cysts of the oral cavity are the result of localized irritation and obstruction. Trauma with subsequent infection originating at the mouths of the ducts and solidifying chemical changes in the secretion of the ducts are the most common etiologic factors. The cysts in most cases can be recognized without difficulty. They gradually increase in size until they rupture spontaneously or become so painful that the patient seeks the advice of a surgeon. In the beginning they are benign and usually sterile, but if they become infected an abscess may result. Malignant disease may follow frequent recurrence or unsuccessful treatment.

Leukokeratosis (Leukoplakia) In the absence of some associated eruption, such as lichen planus, lupus erythematosus or certain fungous processes sometimes found on the oral mucosa, leukoplakia is not difficult to diagnose. Patches may be present on any part of the oral mucosa, my case histories reveal that they most frequently occur first on the mucocutaneous areas of the lips and may extend back from the commissures of the mouth and buccal mucosa even to the hard palate. I have not found the tongue so commonly involved except in cases of proved syphilis. It is generally accepted that the chief etiologic factor in leukoplakia is chronic irritation, the irritating factors may be traumatic, thermal, physicochemical or electrogalvanic. Histologically senile keratosis of the skin and leukoplakia of the oral mucosa are essentially the same.

Hazen and Eichenlaub,⁴ Fox,⁵ and Eichenlaub⁶ have reported clinical and statistical reviews of several hundred cases. Fox⁵ and Eichenlaub⁶ called attention to the comparative infrequency of leukoplakia and cancer of the mouth in the colored races. My own investigations a few years ago among the full-blooded Indians of Oklahoma disclosed 1 case of cancer of the lip beginning with leukoplakia and not a single case of cancer of the mouth, although the Indian is an incessant smoker when economic conditions permit. In spite of the outdoor life and exposure to sunlight, there was not a single case of senile keratosis.

The records of the Lain-Eastland Clinic disclose that leukoplakia, like senile keratoses, appears most often in persons of fair complexion who have not a normal amount of cutaneous pigment. I suggest that chronic irritation, as in cancer, plays only a secondary role in the precipi-

⁴ Hazen, H. H., and Eichenlaub, F. J. *Leukoplakia Buccalis*, J. A. M. A. 79:1487 (Oct 28) 1922.

⁵ Fox, H. *Some Diseases of the Oral Mucosa*, Pennsylvania M. J. 38:465 (April) 1935.

⁶ Eichenlaub, F. J. *Leukoplakia Buccalis*, Arch. Dermat. & Syph. 37:590 (April) 1938.

tation and localization of leukoplakia on the mucosa of those who, by heredity or otherwise, are predisposed to hyperkeratinization of epithelial tissue

I have recently reviewed a series of 178 cases of leukoplakia of the oral mucosa taken from my private case records, with special reference to smoking, wearing of artificial dentures and character of the skin (whether blond or brunet). Ninety-six cases in which such factors were not particularly noted were eliminated. Seventy-seven of the patients in the remaining 82 cases were men, and 5 were women. Seventy-three of the men were smokers, 14 of these wore artificial dentures. Four were nonsmokers, all wore partial or full artificial dentures. Of the 64 men who had fair complexions, 61 showed signs of either superficial or deep senile keratosis on the hands or the face or both. One man, a full-blooded Indian who had leukoplakia of the lower lip which subsequently became a cancer, did not have any senile keratosis. Of the 5 women who had leukoplakia of the mouth, 3 admitted smoking and 4 wore partial or full artificial dentures. Four of the women had fair complexions, and 2 of these had superficial keratosis on the face and hands. One was an Indian woman who smoked and had cancer of the lower lip which had been preceded by leukoplakia, she showed no evidence of senile keratosis.

Cancer. The clinical symptoms of cancer within the oral cavity are so well known to most physicians and the general subject of cancer so large that only brief mention will be permitted in this paper. It is generally accepted that the primary precipitating factor in cancer of the mouth is chronic irritation. The presence of rough, carious or irregular teeth, crude, ill-fitting partial or full artificial dentures, chronic ulcers due to excessive use of tobacco or the warning flag of leukoplakia always demand a careful examination and perhaps a histologic examination. The responsibility resting on both the physician and the dentist to be keenly alert for all such predisposing factors in the mouths of adults cannot be overemphasized.

2 Lesions Due to Mechanophysical Factors—Glossopyrosis. The complex problem of glossopyrosis has been one for occasional mention in medical and dental meetings for many years. Engman⁷ called attention to burning tongue and reported 11 cases, all the patients were between the ages of 35 and 65. He emphasized the overanxiety of these patients about the possibility of cancer. More recently Fox⁸ has made an extensive study, with a review of the literature and a report of 14 cases. Not until recently, however, has there been a series of cooperative studies of this distressing condition by physicians and dentists. The

7 Engman, M. F. "Burning Tongue," *Arch. Dermat. & Syph.* **1** 137 (Feb.) 1920.

8 Fox, H. "Burning Tongue," *New York State J. Med.* **35** 881 (Sept. 1) 1935.

experimental investigations of Kirk,⁹ Goodfriend,¹⁰ Costen¹¹ and others appear to have proved that glossopyrosis may sometimes be caused by chronic irritation of the lingual nerve from abnormal pressure of a loose, overstrained mandibular condyle on its articulation with the temporal bone. The normal articulation of the mandible with the temporal bone consists of a shallow fossa lined with thin cartilage. The inferior division of the trigeminal nerve with its subdivisions of the chorda tympani, the auriculotemporal and the lingual branch lies in close proximity to this joint. The pressure on the surface of the mandibular fossa changes with each position of the mandible during the grinding process of mastication. The degree and direction of pressure on the articular surface vary with the normal or abnormal condition of the molar teeth, which act as a fulcrum. These potent forces acting on the mandibular articulation undergo gradual though marked angular and

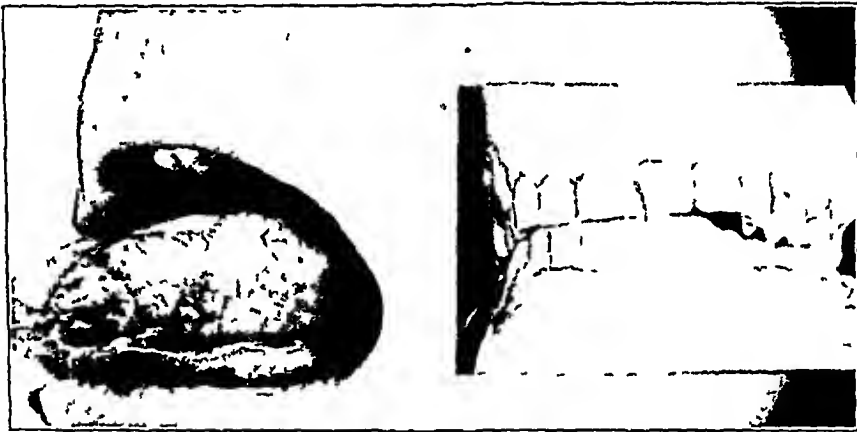


Fig 1—Case in which inversion and malocclusion of molars caused chronic erosion and ulceration of the tongue which eventually became malignant

atrophic changes throughout life. After the loss of coacting molar or other grinding teeth, reconstruction of the denture should be immediately substituted, or abnormal changes in the maxillary processes and mandibular articulations will occur. Dentists admit, however, that the construction of dentures which give perfectly normal pressure balance on the mandibular joint is an ideal rarely attained.

Costen¹¹ has made a study of 90 patients with multiple reflex symptoms in the oral cavity from mandibular malarticulation. Eleven of

9 Kirk, E. C. A Study of the Dynamics Involved in the Evolution of the Human Dentures in the Relation of Centric Occlusion, *Dent Cosmos* 72:631 (June) 1930

10 Goodfriend, D. J. Symptomatology and Treatment of Abnormalities of the Mandibular Articulation, *Dent Cosmos* 75:844 (Sept.), 947 (Oct.) 1933

11 Costen, J. B. Glossodynia. Reflex Irritation from the Mandibular Joint as the Principal Etiological Factor, *Arch Otolaryng* 22:554 (Nov.) 1935

these complained of "burning tongue," and in all instances relief was obtained by means of prosthetic restorations. During my study of oral galvanism I observed numerous cases of "burning tongue." In 2 of these the condition was completely relieved by a dentist who reconditioned the mandibular joint after correction of possible electrogalvanism had failed. I am convinced, therefore, that in addition to the known causes of glossopyrosis a local mechanical factor has been established.

3 *Lesions Due to Physicochemical Factors*—Allergic Reaction to Dentures and Reconstructions. Since the discovery that skilled artisans can mold and construct a serviceable substitute for teeth, dentists and manufacturing supply laboratories have been faced with the major problem of finding a satisfactory basic denture material which would not cause the so-called rubber sore mouth. As in medicine, progress has been characterized by trial and error with many compounds of rubber known as vulcanite, to which various minerals have been added. Modern basic materials, used under various proprietary names, consist essentially of a plastic resinoid formed by a chemical combination of camphor, phenol and formaldehyde.

Discussion of this problem is relatively common in dental literature, but it is not so well known to the members of the medical profession. Within recent years Lindsay,¹² Lain,¹³ Rattner¹⁴ and others have discussed and reported cases of "denture stomatitis" in which the diagnosis was proved by patch testing. This condition is usually caused by an uncured denture which permits dissolution and absorption of certain of its chemical constituents.

Many technical procedures have been proposed for treating basic denture compounds so that their poisonous elements may be fixed and rendered inert. Dentistry has gone far toward a solution of this problem, but individual sensitivity to certain chemicals demands further research.

Sensitivity to Metals. Traub and Holmes¹⁵ have recently reviewed the literature and reported 2 cases of stomatitis and localized dermatitis extending over the chin and portions of the upper part of the chest and caused by sensitivity to the mercury in amalgam fillings.

12 Lindsay, H. C. L. Traumatic Glossitis Due to Irritants Contained in Plastic Denture Materials, *Urol & Cutan Rev* **34** 169 (March) 1930.

13 Lain, E. S. Chemical and Electrolytic Lesions of the Mouth Caused by Artificial Dentures, *Arch Dermat & Syph* **25** 21 (Jan) 1932.

14 Rattner, H. (a) Lesions of the Mouth from Sensitization to Base Plate Material, *J Am Dent A* **23** 1519 (Aug) 1936, (b) Stomatitis Due to Sensitization to Dental Plates, *J A M A* **106** 2230 (June 27) 1936.

15 Traub, E. F., and Holmes, R. H. Dermatitis and Stomatitis from the Mercury of Amalgam Fillings, *Arch Dermat & Syph* **38** 349 (Sept) 1938.

In October 1938 I observed in consultation with a dentist a case of probable silver amalgam poisoning in a girl 12 years old. She had an eruption in the mouth and on the skin similar to that in a case reported by Traub and Holmes except that in our case the dermatitis on the chin and around the mouth strikingly corresponded to the fingerprints of the dentist. The patient's mother reported a similar eruption about eighteen months previously, following the placing of an amalgam filling in another tooth by a different dentist. During my investigation of galvanism in the oral cavity I have several times observed discolored areas on the mucosa which I have attributed to sensitivity to metal rather than to galvanism.

4 *Galvanism*—The subject of galvanism between different metallic restorations has been discussed in dental meetings at intervals for more than half a century, but a review of medical and dental literature fails to disclose a clinical study of this subject until within the last decade. At a meeting of the 'Section on Dermatology and Syphilology' of the American Medical Association in May 1931, I¹³ gave a brief report of a study made by myself and my associates of 30 cases of oral cavities containing dissimilar metallic dentures and briefly discussed symptoms and lesions which might be produced. I have since published three additional studies,¹⁶ including a large series of case reports. The clinical and laboratory investigation which was stimulated by the publication of this work has been flattering.

Venable, Stuck and Beach¹⁷ have since conducted a series of experiments on dogs in which they fractured the radial bones and repaired the fractures by means of metal plates and screws made from various pure and alloyed metals. They demonstrated that body fluids other than saliva contain the necessary elements of a good electrolyte. After four to six weeks the experimental animals were examined, and the chemical, histologic and roentgen findings revealed that a decided degree of electrolysis had occurred between the electropositive and the electro-negative metals. In several cases there was almost total dissolution of the electropositive metals. The ionization of the dissimilar metals, though similar to that which occurs in the human oral cavity, was even more spectacular.

16 (a) Lain, E. S. Electrogalvanic Lesions of the Oral Cavity Produced by Metallic Dentures, *J. A. M. A.* **100** 717 (March 11) 1933, (b) Electric Phenomena in the Oral Cavity, *Dent. Digest* **40** 214 (June) 1934. (c) Lain, E. S., and Caughron, G. S. Electrogalvanic Phenomena of the Oral Cavity Caused by Dissimilar Metallic Restorations, *J. Am. Dent. A.* **23** 1641 (Sept.) 1936.

17 Venable, C. S., Stuck, W. G., and Beach, A. Effects on Bone of the Presence of Metals, Based upon Electrolysis. Experimental Study, *Ann. Surg.* **105** 917 (June) 1937.

The data obtained by my own experiments and those of others are as follows 1 A mouth containing two or more dissimilar metals in the presence of saliva has all the essential factors of a galvanic battery 2 The degree of electric potential between metallic substances in the mouth depends principally on the relation of these substances to each other in the standard electromotive series of metals, although other factors may be involved 3 Discoloration and disintegration of metallic dentures sometimes produce objective and subjective symptoms in the oral cavity

In my series, qualitative spectroscopic examination of tissue removed from the mouth showed that in 9 of the 12 cases observed there was an abnormal content of various electropositive dental metals In the 3

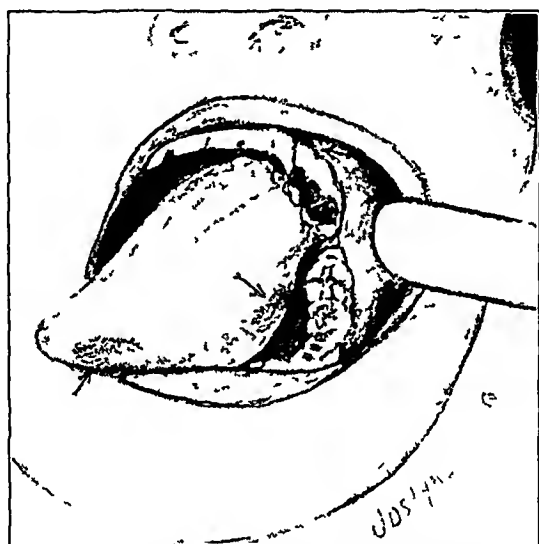


Fig 2—Illustration of the most commonly observed visible irritation of the tongue caused by electrogalvanism between dissimilar metallic dentures and dental restorative materials

remaining cases the condition was probably due to sensitivity to the metals instead of to galvanism Lesions in the oral cavity produced by heterogeneous dental metals are not "galvanic burns" They are the tissue reaction to the localized deposition of certain ionized toxic metals

Recent investigations by Solomon and his collaborators,¹⁸ Miller¹⁹ and others have consisted of electrophysical laboratory studies to determine what tissue or chemical factors constitute the necessary connecting links conducive to a flow of current Many factors of this problem, such as the intrinsic mode of conduction, a more accurate technic of measure-

18 Solomon, H A , Reinhard, M C , and Goltz, H L Salivary Influence on Galvanism, *Dent Items Interest* 60 1047 (Nov) 1938

19 Miller L L Unpublished data

ment and the evaluation of pathologic possibilities, remain unsolved. However, a sufficient number of case reports has now accumulated in the medical and the dental literature to confirm further my earlier conclusion that electrolysis of dental metals constitutes a pathologic entity.

SUMMARY AND CONCLUSIONS

1 The mucosa of the oral cavity is closely related genetically, histologically and sympathetically to the cutaneous structure of the human body, though it is subject to certain additional physical and physicochemical irritating factors.

2 There has not been sufficient cooperative study between physicians and dentists to differentiate systemic from local diseases of the mouth.

3 Physical, mechanophysical or electrogalvanic lesions are not infrequent. They are often attributed to local infections or systemic causes.

4 Irregular and abnormal dental development and subsequent deteriorating changes in the teeth may cause lesions of varying character and degree.

5 Many of the hypertrophies and hyperplasias caused by local physical or physicochemical factors are relatively benign, though leukoplakia and certain other lesions may become malignant and demand prompt and intelligent attention.

6 There is a close relation between racial and other inherent predisposing factors in the occurrence of leukoplakia and senile keratoses.

7 The reaction of the oral mucosa to artificial basic denture materials and metallic restorative substances has constituted a major problem which offers a further challenge for investigation.

8 Electrolysis between electropotentially dissimilar metallic dentures and dental restorative materials presents a new pathologic entity and requires further research for its complete solution.

ABSTRACT OF DISCUSSION

DR HOWARD FOX, New York. Glossodynia, glossopyrosis and burning tongue (a term first used by Engman) are synonymous. Pain in the tongue from organic lesions due to syphilis, tuberculosis, trauma, leukoplakia, Moeller's glossitis or true neuralgia due to involvement of the fifth nerve or occasionally of the glossopharyngeal nerve should not be included under this classification. Burning tongue is not a disease *sui generis* but a symptom which may have many unrelated causes, including mental suggestion, pernicious anemia, with or without changes in the gastric mucosa, and probably avitaminosis. Local causes are of less importance and include the use of tobacco and the presence of jagged teeth. In my published series of 14 cases, burning tongue disappeared completely after cessation of smoking.

DR A. J. MARKLEY, Denver. Dr. Lain has mentioned a form of stomatitis induced by dentures made of improperly cured vulcanite, this condition, known as "rubber sore mouth," rarely appears when the vulcanite is cured for twelve to

twenty-four hours but is not uncommon when the period of curing is reduced to a few hours, and particularly if colored rubber is used. Some base plate substitutes for rubber contain camphor, resinoids, formaldehyde or phenol and frequently provoke a severe stomatitis, even involving the whole mouth in cases of full dentures.

Useful information regarding such conditions may often be gained by inquiry as to recent dental replacements or reconstructions, and dentists are becoming wary of using such material instead of properly vulcanized rubber.

DR ARTHUR M. GREENWOOD, Boston. I should like to mention some work which Dr. Nathansen at the Huntington Clinic has been doing in the administration of estrogen in the treatment of leukoplakia. In a series of 30 cases, he obtained complete cure in 30 per cent, improvement in 30 per cent and no improvement whatsoever in the remainder. The dose used consisted of 200 to 600 units per day. With this dose, it takes one hundred and twenty days to effect a cure. The cure is not permanent, as there is recurrence in about four months. He has not yet worked out the maintenance dose.

DR SAMUEL AYRES JR., Los Angeles. About a week ago my dentist called my attention to a condition he had observed and which appeared to indicate something new in the causation of sore mouth, namely, the solutions which patients have been using to cleanse their dentures. They immerse the dentures at night in a glass or cup containing an antiseptic and give them a perfunctory rinse before putting them into the mouth in the morning, so that the dentures often contain an appreciable amount of the antiseptic, which may be a fairly strong chemical not intended to be used undiluted. In regard to mechanical factors pertaining to lesions of the mouth, in the past year or so I have had several patients with granuloma fissuratum, the classic picture with the folded coin appearance and fissures at the bottom of them. Two of these patients were edentulous. I understand from talking to dentists that this is not uncommon in their experience. These lesions seem to occur more frequently on the upper gum and may be due to the fact that dentures do not fit closely and that friction has something to do with the beginning of the lesion. My third patient was not edentulous, but the lesion began under a bridge which permitted the accumulation of food and was somewhat loose and seemed to be a physical cause of the disease.

DR DUDLEY C. SMITH, University, Va. It is worth while mentioning that these physical and physicochemical agents may be only an exciting factor. This is illustrated by the production of bismuth or mercurial stomatitis in dirty mouths. Larger doses of these drugs can be given a patient with a clean mouth and teeth without producing stomatitis. It has been said, "A good dentist is necessary in the cure of paresis."

Mild or subclinical nutritional abnormalities, especially vitamin B complex deficiencies, may alter the threshold of irritability of the mucous membrane of the mouth to an extent that allows the production of stomatitis by mild irritants.

DR HENRY D. NILES, New York. I should like to say a word about glossodynia. The cases of sore tongue which I have seen have practically all had a background of carcinomatophobia. On questioning the patients, one frequently obtains a history of *some one in the family or among the patient's friends having died of cancer of the mouth*. This is an important point. It may seem somewhat far afield, but I mentioned this finding to a psychiatrist, who agreed that the patient often associates himself or herself with a dead parent. This was particularly true in the case of an old maid whose father died of cancer of the mouth and in whom a painful tongue later developed.

DR EVERETT S LAIN, Oklahoma City Dr Markley has wisely emphasized the fact that even today old-fashioned vulcanite baked for twenty-four hours is the safest base material for artificial dentures There have been a number of cases of stomatitis reported from the new plastic base material I have already seen two such cases It seems that the new product is not any better and perhaps not as good as old-fashioned vulcanite Dr Greenwood mentioned the use of estrogen in the treatment of leukoplakia I was discussing only the mechanical causes of leukoplakia -It is my opinion that leukoplakia most frequently occurs in persons with an inherent predisposition to endocrine disturbances Granuloma fissuratum was mentioned by Dr Ayres I agree with him that it is more common under the wings of the upper dentures

ACTION OF SULFUR-CONTAINING COMPOUNDS IN ARSENICAL AND MERCURIAL POISONING

WITH REVIEW OF THE USE OF SODIUM THIOSULFATE IN DERMATO-
LOGIC PRACTICE AND REPORT OF EXPERIMENTS ON RABBITS WITH
SODIUM THIOSULFATE, SODIUM P-SULFHYDRIL PHENYL SUL-
FONATE AND SODIUM FORMALDEHYDE SULFOXYLATE

KATHLEEN B MUIR, M D

EVANGELINE STENHOUSE, M D

AND

S WILLIAM BECKER, M D

CHICAGO

One of the earliest sulfur-containing compounds to be recommended for use in combating arsphenamine reactions was a proprietary drug called "intramine" (diorthoaminothiobenzene), recommended by McDonough in 1916. According to Stokes,¹ Fraser and Duncan employed contramine, a derivative of intramine, and Greenbaum obtained good results with thiosinamine in doses of 3 grains (0.19 Gm) in 10 cc of water administered intravenously every one or two days. In 1920 Ravaut² noted that oxidation of the arsphenamines increased their toxicity in rabbits. He added sodium thiosulfate to the arsphenamine solution as a reducing agent to counteract the toxic effects of the oxidized material. He also used the drug in the treatment of arsphenamine dermatitis, which he believed might be due to the oxidized drug, and attributed the beneficial action of sodium thiosulfate to its reducing properties. He administered intravenously daily doses of 4 to 15 Gm in a 20 per cent solution.

This work was aided by a grant from the Kuppenheimer Foundation and by a grant from Eli Lilly and Company.

From the Section on Dermatology, School of Medicine of the Division of Biological Sciences, University of Chicago.

The paper was read before the Section on Dermatology and Syphilology at the Ninetieth Annual Session of the American Medical Association at St. Louis, May 18, 1939.

1 Stokes, J H. Modern Clinical Syphilology, Philadelphia, W B Saunders Company, 1934.

2 Ravaut, P. Des traitements internes en dermatologie, Presse med 28 73, 1920.

In 1923 McBride and Dennie^{3a} reported beneficial results from the use of sodium thiosulfate in 7 cases of acute and chronic arsenical and mercurial complications. Immediately after publication of this report the drug came into general use for the treatment of arsphenamine dermatitis and its use was followed by a decrease in the severity and duration of this complication.

PREVIOUS CLINICAL REPORTS ON THE ACTION AND EFFICACY OF SODIUM THIOSULFATE

The beneficial effect of sodium thiosulfate was at first attributed to a supposed combination with the metallic compounds and their elimination in the form of relatively insoluble sulfides. McBride and Dennie^{3a} stated in their first report that sodium thiosulfate converts the salts of arsenic, mercury, lead, bismuth, zinc and copper into the nontoxic insoluble sulfides. However, in their second report^{3b} they interpreted its action as an opposite one when they stated

Therefore this method is based on the absolute fact that sodium thiosulphate will not only neutralize those metallic poisons which are free in the intestinal tract, but that it has the far more important action of rendering those substances soluble and excretable which have been taken up by the body and have been tightly bound by a protein radical.

This enthusiastic report was immediately challenged by Lutz,⁴ who stated that an aqueous solution of sodium thiosulfate seemed to be beneficial when given intravenously to patients with exfoliative dermatitis but that in patients with acute arsenical poisoning the results were disappointing, and that he doubted its efficacy in the treatment of chronic arsenical poisoning. He attributed the enhanced efficacy of the measures for the treatment of mercurial poisoning to improvement in emergency measures adopted before absorption had taken place rather than to the action of sodium thiosulfate. He stated that the immediate injection of sodium thiosulfate into a region infiltrated with arsphenamine aggravated the condition instead of ameliorating it. Owens⁵ lost no time in refuting the foregoing statement, and added "Sodium thiosulfate is as much a specific in mercury poisoning as quinine is in malaria."

3 (a) McBride, W. L., and Dennie, C. C. Treatment of Arsphenamin Dermatitis and Certain Other Metallic Poisonings, *Arch. Dermat. & Syph.* 7:63 (Jan) 1923. (b) Dennie, C. C., and McBride, W. L. Treatment of Arsphenamine Dermatitis, Mercurial Poisoning and Lead Intoxication. Further Observations, *J. A. M. A.* 83:2082 (Dec 27) 1924.

4 Lutz, H. "Arsphenamin Dermatitis, Mercurial Poisoning and Lead Intoxication," *J. A. M. A.* 84:221 (Jan 17) 1925.

5 Owens, P. H. "Arsphenamin Dermatitis, Mercurial Poisoning and Lead Intoxication," *J. A. M. A.* 84:388 (Jan 31) 1925.

Subsequent to the original report by McBride and Dennie,³ many reports on the clinical use of sodium thiosulfate for patients with arsenical dermatitis and metallic poisoning appeared, which were predominantly favorable. Hoffmann⁶ and Hoffmann and Schreus⁷ reported good results in the treatment of arsphenamine dermatitis. Fuss and Dahlmann⁸ reported favorable results in 7 patients. Deussig⁹ added reports on 2 cases of severe arsphenamine eruption in which he obtained considerable benefit. Semon¹⁰ treated 2 patients with mercurial stomatitis, 1 with bismuth stomatitis, 1 with salivation from bismuth, 1 with postarsphenamine jaundice, 1 with acute arsphenamine dermatitis, 1 with mercurial stomatitis and dermatitis and 1 with local infiltration by arsphenamine. All the patients were promptly relieved. In regard to the mechanism, however, he stated

The action of the salt when injected into the circulation containing a metal or an arsenical derivative is an interesting biochemical problem. I find it difficult to accept the theory that an insoluble sulfide is formed.

Kuhn and Reese¹¹ treated patients with postarsphenamine jaundice, polyneuritis after arsenical intoxication and acute mercurial and arsenical poisoning. The administration of sodium thiosulfate was followed by prompt improvement and a variable increase in arsenic in the urine. They interpreted the disappearance of albumin and casts from the urine as probably due to protection of the kidney by the drug.

Lehner¹² reported good results in dermatitis due to arsphenamine and mercury salicylate. He doubted the neutralization theory, since he obtained good results from the treatment of several inflammatory dermatoses in cases in which there was no question of arsenical poisoning. Kristjansen¹³ reported good results from the treatment of late com-

6 Hoffmann, E. Zur Behandlung der Salvarsan Dermatitis mit Natriumthiosulfat, *Dermat Ztschr* **39** 299, 1923.

7 Hoffmann, E., and Schreus, H. T. Natriumthiosulfat als Heilmittel für Salvarsan (und Hg-) Dermatitis, *München med Wchnschr* **70** 1481, 1923.

8 Fuss, S., and Dahlmann, F. Zur Frage der Natriumthiosulfatbehandlung bei Salvarsandermatitis, *München med Wchnschr* **72** 345, 1925.

9 Deussig, R. Zur Behandlung der Salvarsanvergiftung mit Natriumthiosulfat, *Deutsche med Wchnschr* **51** 1824, 1925.

10 Semon, H. C. An Antidote for Arsenic, Bismuth, and Mercury Poisoning, *Brit M J* **1** 662, 1924.

11 Kuhn, H. A., and Reese, H. H. Sodium Thiosulphate in Treatment of Metallic Intoxication, *J A M A* **85** 1804 (Dec 5) 1925.

12 Lehner, I. Natriumthiosulfat in der Therapie der Hautkrankheiten, *Zentralbl f Haut- u Geschlechtskr* **20** 558, 1926.

13 Kristjansen, A. Sodium Thiosulphate in Preventing Harmful Effects of Salvarsan Treatment, *Ugesk f læger* **89** 154, 1927, abstracted, *Brit M J* **1** 93, 1927.

plications of arsphenamine therapy Schamberg and Brown¹⁴ reported favorable results obtained by combining thiosulfate with calcium (another drug which had been used in the treatment of complications of arsphenamine therapy) in the form of calcium thiosulfate Marchbank, Smith and Church¹⁵ reported recovery following ingestion of a supposedly lethal dose of mercury bichloride They administered large doses of sodium thiosulfate by mouth in addition to that given by the intravenous route Haag and Bond,¹⁶ however, observed that both the oral and the intravenous administration of the drug were of no avail in poisoning by solution of potassium arsenite U S P (Fowler's solution)

As is so often the case after the introduction of a new drug, the initial enthusiasm has been followed by an attitude which is lukewarm if not actually skeptical Stokes¹ stated

The uncertainties reflected by these laboratory conflicts have been carried over into the clinics, and while there has been no extended discussion of the matter in the literature that I have been able to find, a number of observers are less convinced of the absolute effectiveness of sodium thiosulphate, orally or intravenously, than they were some years ago I have, for example, been repeatedly impressed with what I thought was actual damage by injections of sodium thiosulphate continued beyond the third to the sixth day of an arsphenamine dermatitis

Beckman¹⁷ said

I believe that most syphilologists are no longer particularly enthusiastic about the efficiency of sodium thiosulphate

Moore¹⁸ probably showed the highest degree of skepticism among syphilologists when he stated

In spite of seven years' experience with it, I have seen no evidence that the drug is of any value whatever, either in arsphenamine dermatitis or in any other type of arsenical or heavy metal intoxication

Even though opinion has been expressed that the drug may be ineffective, the only report of an actually deleterious effect that we could

14 Schamberg, J F, and Brown, M H Some Studies of Calcium Metabolism Discussion of a New Therapeutic Compound, Calcium Thiosulphate, read before the Eighth International Dermatological Congress, Copenhagen, 1930

15 Marchbank, H E, Smith, C H, and Church, H L Mercuric Chloride Poisoning with Recovery Following the Use of Sodium Thiosulphate, J A M A 96 611 (Feb 21) 1931

16 Haag, H B, and Bond, W R Value of Sodium Thiosulphate in Poisoning from Oral Administration of Arsenic, J A M A 88 1219 (April 16) 1927

17 Beckman, H Treatment in General Practice, Philadelphia, W B Saunders Company, 1938

18 Moore, J E The Modern Treatment of Syphilis, Springfield, Ill, Charles C Thomas, Publisher, 1933

find in the literature is that of Frazier,¹⁹ who administered sodium thiosulfate to 2 patients with arsphenamine dermatitis. This treatment was followed by aggravation of the cutaneous lesions and development of vesiculobullous and bullous dermatitis. In 1 patient bronchopneumonia with pleural exudate and acute hemorrhagic nephritis also developed. In commenting on this unusual reaction, Voegtlin and Dyer²⁰ stated that the heating of the solution of sodium thiosulfate for forty-five minutes at 45 pounds' (20.5 Kg.) pressure may have caused a decomposition of the salt. They also suggested the possibility of confusion of the drug ($\text{Na}_2\text{S}_2\text{O}_3$) with sodium hyposulfite ($\text{Na}_2\text{S}_2\text{O}_4$) which is far more toxic and more easily decomposed than is sodium thiosulfate.

PREVIOUS EXPERIMENTAL WORK

In view of the tremendous enthusiasm for the clinical use of sodium thiosulfate, surprisingly little experimental work has been done to determine its efficacy in metallic poisoning in animals.

Mercury and Lead—Haskell, Henderson and Hamilton²¹ found that sodium thiosulfate was inefficacious in mercuric chloride poisoning in dogs. Melville and Bruger²² came to the same conclusion. Young and Taylor²³ found that sodium thiosulfate did not decrease the toxicity of mercury salicylate, succinimide or bichloride in guinea pigs but seemed to decrease the toxicity of potassium mercuritetraiodide to a slight extent. Curtis and Young²⁴ found that the oral administration of 0.5 Gm of sodium thiosulfate per kilogram of body weight to guinea pigs, rabbits and rats previously poisoned by lead did not appreciably affect the excretion of lead. They decided that the slight effect was due to its alkaline reaction and not to any ability to form soluble or insoluble lead compounds.

On the other hand, Hess and Massaro²⁵ reported favorable results in the treatment of rabbits poisoned by mercury bichloride. In rabbits

19 Frazier, C. N. Purpuric Vesiculobullous Dermatitis Subsequent to Injection of Sodium Thiosulfate, *J. A. M. A.* **88** 537 (Feb. 19) 1927.

20 Voegtlin, C., and Dyer, H. A. Arsphenamine-Sodium Thiosulphate Treatment of Experimental Syphilis, *Pub. Health Rep.* **42** 1045, 1927.

21 Haskell, C. C., Henderson, W. C., and Hamilton, J. R. Sodium Thiosulphate in Mercurial Poisoning, *J. A. M. A.* **85** 1808 (Dec. 5) 1925.

22 Melville, K. I., and Bruger, M. Concerning the Alleged Antidotal Action of Sodium Thiosulphate in Mercuric Chloride Poisoning, *J. Pharmacol. & Exper. Therap.* **42** 185, 1931.

23 Young, A. G., and Taylor, F. L. Effect of Sodium Thiosulphate on Mercury Poisoning, *J. Pharmacol. & Exper. Therap.* **42** 185, 1931.

24 Curtis, A. C., and Young, A. G. Studies of the Action of Sodium Thiosulphate in Metallic Intoxication. II. The Effect of Sodium Thiosulphate on the Excretion of Lead, *J. Lab. & Clin. Med.* **13** 628, 1928.

25 Hess, E., and Massaro, A. F. Sodium Thiosulphate in Mercuric Chloride Poisoning, *J. Urol.* **14** 539, 1935.

given mercury bichloride subcutaneously and sodium thiosulfate intravenously, the blood urea was lower than in those treated with mercury bichloride alone. If 1 Gm of sodium thiosulfate per kilogram of body weight was given, death could be prevented twenty-four hours after intoxication but not later than forty-eight hours after the mercury was given.

Inorganic Arsenicals—Young²⁶ treated 6 rabbits with sodium arsenate and sodium thiosulfate, both given intravenously. He stated

Experimental work on rabbits would indicate that the drug has some value in preventing kidney damage in chronic intoxication, but that its value as an antidote when large amounts of arsenic have been injected is questionable.

Scaduto²⁷ gave arsenous acid to frogs, rabbits and dogs and found that subsequent administration of sodium thiosulfate did not change the course of the arsenical poisoning. Oppenheim and Fantl²⁸ gave 0.011 Gm of arsenous acid per kilogram of body weight to white mice subcutaneously, followed by 0.4 Gm of sodium thiosulfate per kilogram. No difference was noted in those so treated and the controls. Mice to which only sodium thiosulfate was given survived. Kuhn and Reese¹¹ administered sodium arsenate to a series of rabbits and to part of them gave sodium thiosulfate. The latter group showed less renal damage than the former. The changes in the liver and spleen were the same in both groups. Hesse²⁹ gave a large number of compounds to 20 rabbits poisoned by inorganic and organic arsenicals. In discussing the toxicity of metallic sulfides, he stated that arsenic and bismuth trisulfides are poisonous but that the trisulfides of cobalt, silver, mercury and antimony are much less so. He used sodium hyposulfite ($\text{Na}_2\text{S}_2\text{O}_4$), sodium trithionate ($\text{Na}_2\text{S}_3\text{O}_6$), sodium thiosulfate, ammonium thiosulphate, ethyl thiosulphate, rongalit (formaldehyde sulfoxylate), strontium thioacetic acid, thiolactic acid, isethionic acid, potassium xanthate, xanthoacetic acid, glucosemercaptol, 2,5-dithiopiperazin, dialanylecystindianhydride, dileucinecystindianhydride and synthetic glutathione. He was not able to demonstrate any protective effect from the substances given. However, he did state that if a sulfide has been shown to be relatively nontoxic, an effort should be made to

26 Young, A. G. Studies of the Action of Sodium Thiosulphate in Metallic Intoxication. I. The Effect of Sodium Thiosulfate on Arsenic Elimination, *J. Lab. & Clin. Med.* **13**: 622, 1928.

27 Scaduto, P. Il tiosolfato di sodio come antidoto dell'acido arsenicoso, *Boll. Soc. ital. di biol. sper.* **6**: 578, 1931.

28 Oppenheim, M., and Fantl, P. Das Natrium thiosulfat in der Behandlung von durch Arsenbindungen verursachten Hauterkrankungen, *Arch. f. Dermat. u. Syph.* **175**: 438, 1937.

29 Hesse, E. Die Entgiftungsmöglichkeiten der Metalle Co, Ag, Hg and As, *Arch. f. exper. Path. u. Pharmacol.* **122**: 354, 1927.

produce it by therapy Kuhn and Loevenhart³⁰ gave approximately the minimum lethal dose of sodium arsenite to rabbits both orally and intravenously, followed by 50 to 100 mg of sodium thiosulfate per kilogram There seemed to be some protection by this method, and they concluded "that thiosulfate had some value in the treatment of arsenic poisoning when the dosage of the latter is approximately the minimum lethal dose, but the results were not very striking"

Organic Arsenicals—Ullmann³¹ gave organic arsenic in the form of neoarsphenamine and neo-silver arsphenamine intraperitoneally and intravenously to guinea pigs, in doses of 0.05 Gm per kilogram of body weight If immediately after, or within the first half hour, 0.1 Gm of sodium thiosulfate per kilogram was given intraperitoneally or intravenously and the dose repeated every six hours, the animals survived, in contrast to the control animals which succumbed On the other hand, Baba³² administered intraperitoneally a lethal dose of arsphenamine to mice, preceded, accompanied or followed by one-half the lethal dose of sodium thiosulfate (about 1.9 Gm per kilogram), and all the animals succumbed

In studying other sulfur-containing drugs, Fujino³³ reported on the protective action of cysteine against lethal doses of arsphenamine and mercury Voegtlin, Dyer and Leonard³⁴ found that the intravenous injection of reduced glutathione inhibited the toxic action of arsenoxide in rats Feeding glutamic acid and cystine also reduced the toxicity, but cysteine was less efficacious than glutathione They concluded that the data indicated that the SH group of glutathione may be regarded as the so-called arsenic receptor of mammalian protoplasm In this connection, Brown and Kolmer³⁵ found experimentally that the therapeutic properties of sodium thiosulfate are dependent on something other than the sulphydryl content of the skin

30 Kuhn, H, and Loevenhart, A S The Antagonism Between Sodium Thiosulphate and Arsenical Compounds, *J Pharmacol & Exper Therap* **25** 160, 1925

31 Ullmann, K Erfahrung ueber Na-thiosulfat bei Salvarsan-schadigungen, *Dermat Wchnschr* **82** 11 and 56, 1926

32 Baba, T An Experimental Study of Treating Salvarsan Intoxication, *Jap J Dermat & Urol* **24** 43, 1924, abstracted, *Zentralbl f Haut- u Geschlechtskr* **16** 106, 1925

33 Fujino, S Neutralizing Action of Cystein Against Salvarsan and Mercurv Intoxication, *Folia pharmacol japon* **10** 14, 1930, abstracted, *Zentralbl f Haut- u Geschlechtskr* **36** 479, 1931

34 Voegtlin, C, Dyer, H A, and Leonard, C S On the Specificity of the So-Called Arsenic Receptor in the Higher Animals, *J Pharmacol & Exper Therap* **25** 297, 1925

35 Brown, H, and Kolmer, J A The Relation of Arsenicals to the Glutathione Content of Animal Tissues, *J Pharmacol & Exper Therap* **35** 417, 1929

INFLUENCE OF SODIUM THIOSULFATE ON THE TRYPANOCIDAL AND SPIROCHETICIDAL ACTIVITY OF ARSENICALS

If the administration of sodium thiosulfate is followed by action on an arsenical already in the body, it might be expected that the therapeutic efficacy of the arsenical might be altered thereby. Kuhn and Loevenhart³⁰ found that sodium thiosulfate inhibited somewhat the trypanocidal action of tryparsamide when 0.325 Gm per kilogram of the former was injected forty-eight hours after the latter drug. An amount as small as 0.050 Gm per kilogram showed no effect. Harrison³⁶ found that a mixture of neoarsphenamine and sodium thiosulfate was as effective therapeutically as the neoarsphenamine alone. Voegtlin and Dyer²⁰ reported that large doses of sodium thiosulfate did not decrease the trypanocidal efficiency of arsphenamine, neoarsphenamine or sulfarsphenamine and did not decrease the spirocheticidal action of sulfarsphenamine.

INFLUENCE OF SODIUM THIOSULFATE ON THE EXCRETION OF ARSENIC

An interesting and important phase of the study of arsenic poisoning is the influence of the administration of sodium thiosulfate on the excretion of arsenic. Its importance lies in the fact that increased excretion has been advanced as evidence of the beneficial action of the drug.

Increase in Arsenic Excretion—Myers, Groehl and Metz³⁷ showed that patients with arsphenamine dermatitis or jaundice excrete a large amount of arsenic in the urine after each injection of sodium thiosulfate. They therefore attributed the beneficial effect in part to removal of the stored arsenic from the body. Myers and his co-workers³⁸ were so convinced of the efficacy of sodium thiosulfate that they reversed their line of reasoning by stating that the increased excretion of arsenic following the administration of sodium thiosulfate was evidence of the arsenical causation of the presenting dermatosis (usually some form of scleroderma). Ayres and Anderson³⁹ studied 49 cases of various dermatologic conditions in which arsenic was suspected of being a causative factor and in which determinations of the urinary arsenic were made by the Gutzeit method before and immediately after a single

36 Harrison, L. W. Effect of Sodium Thiosulphate on the Therapeutic Power of Arsphenamine Compounds, *Lancet* 1 1161, 1925.

37 Myers, C. N., Groehl, M. R., and Metz, G. P. Therapeutic Activity of Sodium Thiosulphate, *Proc Soc Exper Biol & Med* 23:97, 1925.

38 Myers, C. N., Marples, E., Groehl, M., and Throne, B. The Use of Sodium Thiosulphate in Diagnostic Procedures, *J Lab & Clin Med* 11 836, 1926.

39 Ayres, S., Jr., and Anderson, N. P. Sodium Thiosulphate and the Elimination of Arsenic, *J A M A* 110:886 (March 19) 1938.

injection of sodium thiosulfate (1 Gm in 10 cc of water) They observed that an increase in the urinary excretion of arsenic usually followed the injection of sodium thiosulfate Kuhn and Reese⁴¹ observed varying increases in urinary arsenic after the administration of sodium thiosulfate

Further evidence that sodium thiosulfate increases the elimination of arsenic was claimed by Osborne,⁴⁰ who used the method of Justus as modified by Brunauer and himself to demonstrate supposed crystals of arsenic sulfide in the tissues A remarkable reduction in the quantity of these crystals was seen after the injection of sodium thiosulfate Tannenholz and Muir⁴¹ and Oppenheim and Fantl,⁴² working independently, came to the conclusion that the crystals demonstrated by the method were not those of arsenic sulfide, so that considerable doubt has been cast on the evidence for the increased excretion of arsenic as demonstrated by this method

Decrease or No Increase in Arsenic Excretion—On the other hand, an approximately equal number of investigators have been unable to confirm the increased excretion of arsenic following the administration of sodium thiosulfate, but on the contrary most of them found an actual decrease in excretion Kuhn and Loevenhart³⁰ observed that sodium thiosulfate reduced the total output of arsenic for twenty-four hour periods in animals poisoned with sodium arsenite, and, owing to diuresis, the amount in each cubic centimeter of urine was greatly reduced Mattice and Weisman⁴³ demonstrated an actual decrease in urinary excretion of arsenic after the administration of sodium thiosulfate Oppenheim and Fantl²⁸ studied 13 patients who had received arsenic at various times, most of them shortly before the study was made After arsenical treatment had been discontinued, a twenty-four hour specimen of urine was examined for arsenic by the method of Gangl and Sanchez Sodium thiosulfate was given to 9 of the patients, and another twenty-four hour specimen was examined One patient showed an increase of 106 per cent, but the remainder showed decreases in amounts of as much as 60 per cent The authors explained all the results by the normal daily variation in urinary arsenic and stated the belief that injection of sodium thiosulfate had no effect on the urinary excretion of arsenic

40 Osborne, E D Microchemical Studies of Arsenic in Arsenical Dermatitis, Arch Dermat & Syph 18 37 (July) 1928

41 Tannenholz, H, and Muir, K B Methods for Microchemical Demonstration of Arsenic in Tissues, Arch Path 15 789 (June) 1933

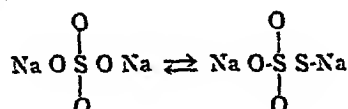
42 Oppenheim, M, and Fantl, P Ueber Hauterkrankungen verursacht durch arsenhaltige Wandfarben II Versuche zum histologischen Nachweis von Arsenverbindungen in der Haut, Arch f Dermat u Syph 170 488, 1934

43 Mattice, M R, and Weisman, D Urinary Excretion of Arsenic I Normal Subjects, Am J M Sc 193 413, 1937

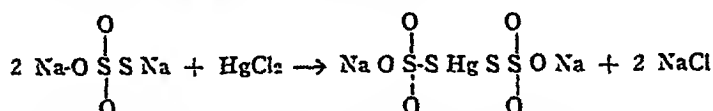
EXPERIMENTS WITH SODIUM THIOSULFATE AND SODIUM
P-SULFHYDRIL PHENYL SULFONATE

In view of the conflicting results, it was decided to restudy some phases of poisoning of animals with metallic salts and the effect of various possible antidotes

When sodium thiosulfate

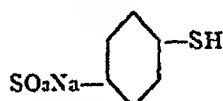


combines with metals, it probably combines in the second tautomeric form Thus, with mercury bichloride (HgCl_2) it will yield

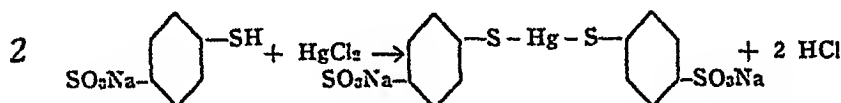


In this molecule, the mercury is little ionized, and forms a very stable bond Most heavy metals probably combine with sodium thiosulfate in this manner

Sodium p-sulfhydryl phenyl sulfonate



will combine with heavy metals in this manner



Inorganic Arsenical—The work of Young ²⁶ was repeated, with the same doses and with some modification of the doses of sodium arsenate in the various series Sodium arsenate was given intravenously in a 10 per cent aqueous solution The sodium thiosulfate was dissolved immediately before use, but the sodium p-sulfhydryl phenyl sulfonate had been put in ampules in aqueous solution Both were given in 5 per cent strength Later, the sodium arsenate was used in a 5 per cent solution, so that the solutions would be of uniform concentrations

Series 1 As controls, 4 rabbits were inoculated with 0.025 Gm of sodium arsenate per kilogram of body weight They lived one, four, eight and sixty days, respectively One animal was given the same dose of sodium arsenate with 0.05 Gm of sodium thiosulfate per kilogram and lived one day A second animal was given 0.03 Gm of sodium arsenate per kilogram with 0.05 Gm of sodium thiosulfate per kilogram The same dose of arsenic was repeated in ten and seventeen days without the thiosulfate The animal lived sixty-three days after the first injection

Series 2 In this series 5 control animals were given 0.025 Gm of sodium arsenate per kilogram of body weight, followed by 0.015 or 0.025 Gm a week later One rabbit died in three days, but the remaining 4 survived for over fifty days Six rabbits were given 0.025 to 0.03 Gm of sodium arsenate per kilogram, followed by 0.015 to 0.03 Gm at weekly intervals Sodium p-sulfhydryl phenyl sulfonate in a dose of 0.05 Gm per kilogram was given on the same day or the

day following the first injection and the dose repeated at intervals of two weeks. Two animals survived for eleven and seventeen days, respectively, and the remaining 4 lived for over sixty days.

Series 3 Owing to the large percentage of survivors in the second series, the dose of sodium arsenate was increased in the third series. As controls, 6 rabbits were given 0.033 Gm of sodium arsenate per kilogram of body weight, followed by 0.02 Gm per kilogram on the following day. Four survived two days, 1 three days and 1 over sixty days after the initial injection. Five rabbits were given the same amount of sodium arsenate with 0.05 Gm of sodium thiosulfate per kilogram on the same day or the day following the first injection, and this was repeated every week or two. Three survived two days, 1 three days and 1 over sixty days.

As controls, 4 rabbits were given 0.04 Gm of sodium arsenate per kilogram of body weight and the same amount on the following day. Three survived one day and 1 two days. Three rabbits were given the same amount of sodium arsenate (0.04 Gm per kilogram), followed by 0.05 Gm of sodium thiosulfate, and they died on the following day.

Series 4 The dose of sodium arsenate was again decreased, owing to the high mortality. As controls, 8 rabbits were given 0.029 Gm of sodium arsenate per kilogram of body weight, and six days later those that survived received 0.0175 Gm per kilogram. Three lived one day and 1 each lived two, three, four, seven and over sixty days. Four rabbits were given 0.035 Gm of sodium arsenate per kilogram, and this dose was repeated eleven days later for the survivors. Two lived one day, 1 two days and 1 thirteen days.

Three rabbits were given 0.029 Gm of sodium arsenate per kilogram of body weight and 0.05 Gm of sodium thiosulfate per kilogram on the same or following day. Two lived one day, 1 two days and 1 over sixty days. To the last animal, 0.0175 Gm of sodium arsenate per kilogram was given every week or two, with 0.05 Gm of sodium thiosulfate per kilogram at the same intervals for one month. Four rabbits were given 0.035 Gm of sodium arsenate and 0.05 Gm of sodium thiosulfate per kilogram and survived one day.

Since theoretically the maximum neutralization of the amount of sodium thiosulfate given to the animals, 0.05 Gm per kilogram of body weight, would be for only one half to two thirds of the sodium arsenate injected, it was increased four-fold. Three rabbits were given sodium arsenate in doses of 0.04 Gm per kilogram and immediately thereafter 0.2 Gm per kilogram of sodium thiosulfate, the latter repeated daily for three days for the survivors. Those treated with thiosulfate died in one, two and three days, respectively. Two controls died in one day and 1 in twenty-nine days.

In these experiments it is doubtful whether any protection was afforded by either sodium thiosulfate or sodium p-sulfhydryl phenyl sulfonate with the method used. Microscopic study of sections from the kidneys and livers of the animals which succumbed showed necrosis and tissue destruction, which did not vary in the animals that had received the arsenate alone and in those which had also received a sulfur compound. These findings are in contrast to those of Kuhn and Reese.¹¹

Organic Arsenical—Rabbits were given neoarsphenamine in single doses and in divided doses. As controls, 3 animals were given 0.20 Gm per kilogram of body weight intravenously. They lived eleven, fifteen and over forty days, respectively.

Three more were given the same amount of neoarsphenamine, followed by 0.05 Gm of sodium thiosulfate per kilogram. They lived eleven, thirteen and over forty days, respectively. Three others were given a like dose of neoarsphenamine, followed by 0.05 Gm of sodium p-sulfhydryl phenyl sulfonate per kilogram. They lived four, thirteen and over forty days, respectively.

In order to test the effect of repeated doses, 3 rabbits for control were given 0.15 Gm of neoarsphenamine per kilogram, and the dose was repeated in nine days for the survivors. One lived three days and 2 over thirty days. Of animals receiving a like amount of neoarsphenamine along with 0.05 Gm per kilogram of sodium thiosulfate per kilogram, 2 survived five days and 1 six days. Of those treated in the same way with sodium p-sulfhydryl phenyl sulfonate, 1 lived for eleven days and 2 for over thirty days.

In view of the relatively small doses of sodium thiosulfate, the experiment was repeated with the amount increased fourfold. For control, 3 rabbits were given 0.025 Gm of neoarsphenamine per kilogram, and the dose was repeated in six days and increased to 0.30 Gm eight days thereafter. One lived seventeen days and 2 over thirty days. Sodium thiosulfate was given to 3 rabbits similarly treated for three days in doses of 0.20 Gm per kilogram, and the dose was repeated once at each subsequent injection. One survived eight days and 2 twenty-three days.

EXPERIMENTS WITH SODIUM FORMALDEHYDE SULFOXYLATE

The protective power of sodium formaldehyde sulfoxylate was demonstrated by Rosenthal⁴⁴ in acute mercurial poisoning in dogs and rats in 1933. Given intravenously to rats it is protective only if administered previous to the poisoning by mercury bichloride. Dogs given mercury bichloride by mouth are protected from death if the sulfoxylate is given intravenously shortly afterward, as the absorption from the gastrointestinal tract does not occur at once and so the nephrotoxic action of the drug is delayed. However, the intravenous administration of the sulfoxylate does not eliminate the corrosive action of the mercury on the gastric mucosa, so that an oral dose of sulfoxylate is also advisable when poison has been taken by mouth. The drug is too irritating to be injected subcutaneously.

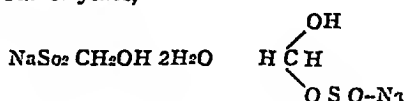
Modell and his co-workers⁴⁵ gave sodium formaldehyde sulfoxylate both intravenously and orally to cats which had been poisoned with mercury bichloride by the same route. Two thirds of the animals recovered when the sulfoxylate was given before a minimum lethal dose of mercury. It was found that the end product of reduction of mercury bichloride with sulfoxylate was toxic on injection, although less so than mercury bichloride. In the oral experiments a high degree of protection resulted if the sulfoxylate was given as soon as one to two minutes after the mercury, but no protection was evident after

44 Rosenthal, S. M. Experimental Studies on Acute Mercurial Poisoning, Pub. Health Rep. 48:1543, 1933.

45 Modell, W., Gold, H., Winthrop, G. J., and Foot, E. B. Sodium Formaldehyde Sulfoxylate in Experimental Poisoning by Mercuric Chloride, J. Pharmacol. & Exper. Therap. 61:66, 1937.

fifteen minutes had elapsed. The acid of the stomach content delayed the reduction process, which was accelerated by the addition of sodium bicarbonate. The product of reduction was found not to be highly toxic when given orally.

Sodium formaldehyde sulfoxylate,



is a powerful reducing agent. It will reduce mercury bichloride (HgCl_2) to metallic mercury.

The following experiments were carried out for the purpose of determining the protective action of sodium formaldehyde sulfoxylate in the poisoning of rabbits by mercury and arsenic.

Mercurial—Mercury bichloride was given intravenously in a 1 per cent solution in doses of 0.025 Gm. per kilogram of body weight, which is the minimum lethal dose for rabbits. The sulfoxylate was given in a 40 per cent solution, in doses of 1 Gm. per kilogram. For control, mercury bichloride was given intravenously to 7 rabbits. Six of them died in four days (on an average), and 1 was alive at the end of two months. Seven rabbits were given the same dose of mercury bichloride which was followed in one-half to one and one-half minutes by the sodium formaldehyde sulfoxylate. Six died in three to four days, and 1 was living at the end of two months. In 7 other rabbits, the sulfoxylate was given first and the mercury bichloride five minutes later, all animals were alive at the end of two months.

Inorganic Arsenical—As controls, 3 rabbits were given 0.04 Gm. per kilogram of sodium arsenate by the intravenous route. Two survived one day, and 1 twenty days. Three rabbits were given 1 Gm. of sodium formaldehyde sulfoxylate per kilogram, followed in five minutes by 0.04 Gm. of sodium arsenate per kilogram. All animals died on the following day.

Organic Arsenicals—Six rabbits were given intravenously 0.20 Gm. per kilogram of a 10 per cent solution of thioarsene,⁴⁶ followed immediately by 1 Gm. of sodium formaldehyde sulfoxylate per kilogram in a 20 per cent solution. At the end of ten days 5 were dead and 1 was alive. In a second series of 6 rabbits, physiologic solution of sodium chloride was substituted for the sulfoxylate. At the end of sixteen days 3 were alive and 3 were dead. A third series of 6 rabbits, controls, were treated with thioarsene alone. At the end of thirteen days 5 were dead and 1 was alive.

In order to test the influence of sodium formaldehyde sulfoxylate when administered before the injection of an organic arsenical, 3 rabbits were given 1 Gm. per kilogram of a 20 per cent solution of sodium formaldehyde sulfoxylate, followed in five minutes by 0.20 Gm. of neoarsphenamine per kilogram. These doses were repeated in six days, and eight days thereafter the sodium formaldehyde sulfoxylate was followed by 0.3 Gm. of neoarsphenamine per kilogram. The animals died in sixteen, twenty and twenty-three days, respectively, while 1 control died in seventeen days and 2 in over thirty days.

46 Eckler, C. R., and Shonle, H. A. A Preliminary Study of Thio-Arsene, Disodium Bis-(p-Sulfophenyl) (Acetamidophenyl) Dithio-Arsenite, *Am. J. Syph.* 19: 495, 1935.

RESULTS OF EXPERIMENTAL STUDIES

It is of course understood that animals do not manifest the varying degrees of hypersensitiveness to various arsenical and mercurial compounds which are seen occasionally in human beings. The rabbits which were given sodium arsenate in varying doses and at varying intervals were protected by neither sodium thiosulfate nor sodium p-sulfhydryl phenyl sulfonate as given in the experiments. Any differences could be accounted for by the limits of experimental error. In the case of neoarsphenamine, the animals to which sodium thiosulfate was given lived a somewhat shorter time than those which received neoarsphenamine alone or neoarsphenamine followed by sodium p-sulfhydryl phenyl sulfonate. A protective action against mercury bichloride poisoning in rabbits was demonstrated only if sodium formaldehyde sulfoxylate was given before the mercury salt. In the case of inorganic and organic arsenicals, it did not protect from poisoning by sodium arsenate or neoarsphenamine when given before the arsenical or from thioarsene when given afterward.

These findings are in conformity with most of the previous experimental work, the results of which have been largely unfavorable. The one exception is the use of sodium formaldehyde sulfoxylate before poisoning animals with mercury bichloride, for which favorable results have always been reported.

PHARMACOLOGY OF SODIUM THIOSULFATE

Since the clinical reports of the use of sodium thiosulfate have been for the most part encouraging, and since it has been assumed by many clinicians that the beneficial results are due to elimination of arsenic or other metal by the drug, it may be well to discuss the pharmacologic properties and some of the theories as to the action of sodium thiosulfate.

According to Heffter and Heubner,⁴⁷ sodium thiosulfate crystallizes with five molecules of water in large prisms. It dissolves in 1 part of water at 15 C, producing a weakly alkaline solution. It is a strong reducing agent. They stated that little pharmacologic work has been done with the drug. It is relatively nontoxic. Lasch⁴⁸ stated that it may be consumed orally without harm up to 15 Gm per day but added that in this dose it would produce catharsis and possibly emesis. Voegtlin and Dyer²⁰ stated that in experiments with rabbits doses of 1 to 2 Gm per kilogram of body weight in a 10 per cent solution,

47 Rost, E. Schweflige Säure, in Heffter, A., and Heubner, W. Handbuch der experimentellen Pharmakologie, Berlin, Julius Springer, 1927, vol 3, pt 1, p 416

48 Lasch, cited by Sollmann, T. A Manual of Pharmacology, Philadelphia, W B Saunders Company, 1936

injected slowly into an ear vein, were tolerated without the production of any symptoms. Higher doses (4 Gm per kilogram) produced restlessness toward the end of the injection, followed by muscular weakness and depression. Baba³² gave sodium thiosulfate to mice in doses of 2.5 to 7 Gm per kilogram. Over 3.8 Gm per kilogram resulted in death in four hours. The kidneys increased in volume and became hyperemic, and the vessels were dilated and hemorrhagic. When one half to two thirds of the lethal dose was given daily for one week, almost all the animals lived, though they had swollen kidneys. Nyiri⁴⁹ stated that sodium thiosulfate is partially (60 to 70 per cent) oxidized to sodium sulfate, with liberation of sulfur, and 30 to 40 per cent is excreted unchanged in the urine.

Attention has been repeatedly called to the fact that the drug should be chemically pure, and many workers have emphasized the necessity of making up a fresh solution for each intravenous injection. Voegtlin and Dyer²⁰ cautioned that the drug must not be autoclaved and also that sodium thiosulfate ($\text{Na}_2\text{S}_2\text{O}_3$) must not be confused with sodium hyposulphite ($\text{Na}_2\text{S}_2\text{O}_4$), which is far more toxic and more easily decomposed. Kharasch⁵⁰ stated that there should be no decomposition in well ampuled solutions of sodium thiosulfate, and several workers, among them Ayres and Anderson,³⁰ stated that they have experienced no difficulty with ampuled solutions.

The recommended doses for intravenous administration of the drug have not varied a great deal. McBride and Dennie^{3a} recommended 0.3 Gm on the first day, 0.45 Gm on the second, 0.6 Gm on the third, 0.9 Gm on the fourth, 1.2 Gm on the sixth and 1.8 Gm on the eighth day. In acute poisoning from mercury bichloride taken by mouth, they gave 15 Gm in 480 cc of water by mouth, followed by 1 Gm intravenously, three times daily. Most authors recommend that only a few injections be given. Stokes¹ believed that the drug should not be given for more than three to six days in arsphenamine dermatitis.

THERAPEUTIC ACTION OF SODIUM THIOSULFATE

There is no agreement as to the therapeutic action of sodium thiosulfate in complications from metallic poisoning. The various theories which have been presented, with evidence that has been advanced in their favor or against them, are

1 *Reduction*—Ravaut² first used the drug, adding it to arsphenamine for its reducing effect, in order to prevent oxidation to arsenoxide, which would increase the toxicity. He also gave the drug intravenously to reactive patients, evidently with the idea of utilizing its reducing

49 Nyiri, cited by Myers and others³⁸

50 Kharasch, M. S. Personal communication to the authors

action It has since been shown that the drug would have little or no reducing action except in an acid medium, which does not exist in the body, so that it cannot act in this manner

2 *Alkalinization*—Curtis and Young²⁴ concluded that the slight increase in excretion of lead after administration of sodium thiosulfate results from the latter's alkaline reaction The solution usually administered (10 per cent) is a neutral solution, and even a solution containing the drug in high concentration is only slightly alkaline Shaffer⁵¹ stated that administration of the drug should not be continued indefinitely, since it has a tendency to produce alkalosis The manner of its action in this regard is not clear

3 *Diuresis*—Baba³² stated that in mice poisoned with arsphenamine there was no neutralizing effect on the arsphenamine, but a diuretic action Fuss and Dahlmann⁸ noted an increase in the output of water both by the kidneys and the skin in patients with arsphenamine dermatitis associated with severe edema who had been given sodium thiosulfate Kuhn and Loevenhart³⁰ noted diuresis after administration of sodium thiosulfate to animals poisoned by sodium arsenite

4 *Formation of Less Toxic Metallic Sulfides*—McBride and Dennie,^{3a} who introduced sodium thiosulfate in this country, originally attributed its action to formation of sulfides which are less toxic than the original material Considerable work has been done on this problem, and the majority of opinions is against such a conception of the drug's action as far as the interior of the body is concerned Kuhn and Loevenhart³⁰ stated that sodium thiosulfate forms a less toxic compound with the metallic salts Scaduto²⁷ mixed solutions of sodium thiosulfate and arsenous acid at room temperature and at 38 C and also boiled the mixture Metallic sulfide was not formed even in the presence of an excess of sodium thiosulfate It was only when the medium was made acid (p_H 4.5) that the arsenic sulfide was formed, i e, only when nascent sulfur was released from the sodium thiosulfate This finding would seem to justify an effort to neutralize poisons taken orally by administering sodium thiosulfate by mouth, since the content of the stomach is acid, but makes it highly improbable that arsenic sulfide would be formed in the body It must be remembered, however, that some metallic sulfides are poisonous, while others are relatively innocuous Meneghetti⁵² found that colloidal arsenic sulfide, given by mouth, is about as toxic as arsenous acid He stated that if arsenic sulfide is formed in the body, it would be in the colloidal form Hesse²⁹

51 Shaffer, L W Treatment of Post Arsphenamine Dermatitis, Arch Dermat & Syph. 29:173 (Feb) 1934

52 Meneghetti, cited by Scaduto²⁷

showed that arsenic and bismuth trisulfides are poisonous, but cobalt, silver, mercury and antimony sulfides are much less toxic. It would therefore seem more logical to administer sodium thiosulfate by mouth in mercurial poisoning than in arsenical poisoning, since the mercury sulfide which would be formed is relatively nontoxic compared with mercury bichloride, the substance usually ingested. As stated previously, Semon found it difficult to accept the theory that an insoluble sulfide is formed.

The predominance of negative experimental results in animals over the few positive results is against the probability of the formation of metallic sulfides in human beings. If such action takes place in man, it should take place also in animals, since their tissues have so many chemical similarities.

5 *Rendering Metallic Salts Soluble and Excretable*—This action was emphasized in the second report of Denmie and McBride,^{3b} without evidence being reported, but has not been considered by any authors since that time. The increased excretion of arsenic and mercury after administration of the drug might be used as an argument in favor. However, about 50 per cent of the reports on excretion fail to indicate any increase, so that the question must be considered as still open.

A weighty argument against direct action on the arsenic itself, as illustrated by theories 4 and 5, is advanced by Lehner,¹² who obtained as good results in nonarsenical as in arsenical dermatitis.

6 *Intravital Formation of Sulfur*—Moore¹⁸ called attention to the belief that has prevailed for many years that sulfur is an antidote for metallic poisoning. Nyiri⁴⁰ found that sulfur is liberated in the body from sodium thiosulfate, but Scaduto²⁷ expressed doubt that this occurs. Koch⁵³ stated that the action of sodium thiosulfate may be due to its sulfur content. Sollmann⁵⁴ stated

It appears to be successful against the dermatitis and the arsenical jaundice, but the evidence for the mechanism of its action is not known. Since thiosulphate has a similar beneficial effect on non-arsenical and non-metallic dermatitis, it is quite conceivable that the action is not on the arsenic, but that it is perhaps an allergic response to the precipitation of colloidal sulfur.

When injected into an area infiltrated with arsphenamine, however, he believed that the effect was simply that of a diluent.

Oppenheim and Fantl²⁸ stated that the good results from sodium thiosulfate were due to the breaking off of sulfur in the body and that the effect had nothing to do with arsenic itself. He called attention

53 Koch, F. C. Personal communication to the authors.

54 Sollmann, T. A Manual of Pharmacology, Philadelphia, W. B. Saunders Company, 1936.

to the fact that disturbances in carbohydrate and protein metabolism are often observed in patients with arsphenamine dermatitis. The use of sulfur waters internally is said to increase the formation of glycogen in the liver. One gathers from the more recent method of treating arsphenamine complications, by means of dextrose,⁵¹ that the action has something to do with the liver. It may well be that the result is similar to that reported for sulfur and perhaps obtained by injection of sodium thiosulfate.

Mueller and Delbanco⁵⁵ classified the injection of sodium thiosulfate as sulfur therapy but had a different explanation for its action. They stated that the point of action of the drug was unknown but its administration removed the irritability of the sympathetic nervous system, permitting resumption of normal regulation and restoration of skin tonus and function. They quoted Schuster as having demonstrated increased excretion of mercury after sulfur baths. Other physicians specializing in baths have claimed an increase in general metabolism from the same source. Mueller and Delbanco attributed arsenical dermatitis to a secondary action through the vasomotor system. As a result, the skin is not able to resist irritation, including that from arsenic in amounts which would ordinarily cause no trouble. After administration of sodium thiosulfate the function of the skin improves and arsenic is liberated.

As regards other possible methods of therapeutic action of sodium thiosulfate, Brown and Kolmer³⁵ found experimentally that the therapeutic properties of sodium thiosulfate are dependent on something other than the sulfhydryl content of the skin.

ACTION OF SODIUM FORMALDEHYDE SULFOXYLATE

It is generally agreed that sodium formaldehyde sulfoxylate acts *in vivo* by its power of reducing mercury bichloride, whereby it forms a less toxic mercurial compound. Reduction also takes place *in vitro*, and the resulting substance has been shown⁴⁵ to be less toxic when administered to animals than the original salt.

COMMENT

From the foregoing review it is seen that a great deal of apparently contradictory evidence has been presented. It must be remembered, however, that different compounds and different animals have been used by the various investigators, and various methods of administration of sodium thiosulfate have been employed. From the data presented, it may be assumed that there is little if any evidence that sodium thiosulfate

⁵⁵ Mueller, E. F., and Delbanco, E. Zur Schwefeltherapie in der Venereologie und Dermatologie, *Zentralbl. f. Haut- u. Geschlechtskr.* 20:398, 1926.

acts on arsenical or mercurial salts to form sulfides in the body, owing to the improper p_H , although the acidity of the stomach is such that a sulfide may well be formed there if the drug is given orally for poisoning by ingestion. There would be little advantage in giving sodium thiosulfate by mouth in arsenical poisoning, to substitute the relatively toxic arsenic sulfide for some other arsenical salt, but mercury sulfide is so relatively nontoxic that the administration of sodium thiosulfate by mouth should be of distinct help if made early.

According to Kharasch,⁵⁶ sodium thiosulfate, or any similar sulfur compound, should not act on an arsenical with a double bond between the two arsenic atoms, such as is present in arsphenamine. However, after arsenoxide has been formed in the body, the double bond has been broken, and such action could theoretically take place. In the body tissues, however, the p_H is not correct for sodium thiosulfate, since it combines only in an acid medium, but sulfhydryl derivatives could be effective, as was shown for glutathione.⁵⁴ Our negative results with sodium p-sulfhydryl phenyl sulfonate may have been due to the method of administration, whereby the drug was not present at the time arsenoxide was produced in the animal from the breaking down of neo-arsphenamine. This phase of the problem suggests the possible value of glutathione or other sulfhydryl compound in poisoning by an overdose of arsenoxide (mapharsen).

A valid argument could be raised that the reduction of the severity and duration of arsphenamine reactions has been so definite in many countries since the introduction of sodium thiosulfate that the drug must be responsible. There are at least two other factors of possible participation in this change. At the same meeting at which McBride and Dennie⁵⁵ made their first presentation, Stokes and Cathcart⁵⁷ emphasized the importance of focal and intercurrent infections in the production of arsphenamine reactions. Since that time, more attention has been paid to the elimination of foci of infection previous to arsphenamine therapy, and greater care has been taken to make certain that the patient is not febrile at the time of administration of this drug. A second factor, for which there is no absolute evidence, is the possibility that manufacturers have achieved an improvement in the chemical purity of arsphenamine, resulting in fewer reactions. Against this assumption is the fact that favorable reports emanated from several countries, and it is illogical to assume that a sudden change in the drug would have occurred simultaneously over such a large territory. On the

56 Kharasch, M. S. Personal communication to the authors.

57 Stokes, J. H., and Cathcart, E. Contributory Factor in Post-Arsphenamin Dermatitis, with Special Reference to the Influence of Focal and Intercurrent Infection, *Arch. Dermat. & Syph.* 7:14 (Jan.) 1923.

basis of an analysis of the possible mechanisms of action of sodium thiosulfate it would seem, from the evidence presented, that the most logical conception of its action is that of the intravital formation of sulfur. This suggests the advisability of further study of the sulfur problem in combating reactions from arsenic and mercury. Diuresis has been regularly reported and may also play a role.

SUMMARY

The literature is reviewed relative to the clinical and experimental evidence for the value and action of sodium thiosulfate and other sulfur-bearing compounds and sodium formaldehyde sulfoxylate in poisoning by various metallic salts, especially arsenic and mercury.

Studies carried out on 123 rabbits poisoned with inorganic and organic arsenicals and mercury failed to show any protective action of sodium thiosulfate or sodium p-sulfhydryl phenyl sulfonate, as used in various ways. Microscopic examination of the kidneys of animals poisoned by sodium arsenate showed the same degree of degeneration regardless of whether sodium thiosulfate or sodium p-sulfhydryl phenyl sulfonate had been given.

The pharmacology of sodium thiosulfate is presented. It is a safe drug to use in the recommended dosage.

Analysis of the possible modes of action of sodium thiosulfate—reduction, alkalization, diuresis, formation of less toxic metallic sulfides, rendering metallic salts soluble and excretable and intravital formation of sulfur—suggests the probable action by intravital formation of sulfur, a substance which has long been used in the treatment of metallic intoxication.

Theoretically, sodium p-sulfhydryl phenyl sulfonate should have a more definite action on arsenicals because of its sulfhydryl group, but this was not demonstrated in the experiments performed.

Sodium formaldehyde sulfoxylate protected rabbits poisoned with mercury bichloride only when given before the latter and not when given afterward. It had no protective action against poisoning by inorganic and organic arsenicals, regardless of whether it was given before or afterward.

Sodium formaldehyde sulfoxylate acts by reducing mercury bichloride to metallic mercury, which is considerably less toxic. It protects only when given previous to the mercurial salt when the latter is administered by the intravenous route. When the mercurial salt is given by mouth the protective drug must be administered only a few minutes thereafter. If the latter is given orally for mercurial poisoning by ingestion, it should be given with sodium bicarbonate, to counteract the effect of the gastric acid, which delays reduction of mercury salts.

ABSTRACT OF DISCUSSION

DR CHARLES C DENNIE, Kansas City, Mo In 1933 McBride and I published the first paper in this country on the use of sodium thiosulfate in the treatment of arsenical dermatitis, lead poisoning and mercury poisoning In those days we knew nothing whatsoever of the nine day erythema of Milian, and many of the patients we treated at that time we now recognize as being of that group which would have recovered spontaneously had no treatment been given Yet, after all these years of administering sodium thiosulfate, though its action cannot be explained chemically, I still feel that it has a place in the treatment of arsenical dermatitis After two or three years during which we received both favorable and unfavorable criticism, we began to question the efficacy of sodium thiosulfate, so we decided to do some experimental work ourselves We have never published the results except in one paper, "The Toxic Action of Sodium Thiosulphate" We decided to see whether sodium thiosulfate would protect dogs against the poisonous effects of mercury bichloride Goldblatt worked with me and afterward published a paper on the treatment of mercurial poisoning with sodium thiosulfate

We found that we should give these dogs mercury in the same way that a human being would take it, that is, by mouth So we gave each dog $7\frac{1}{2}$ grains (0.48 Gm) of mercury bichloride in that manner If we washed out the stomach with plain water before twelve minutes, the dog did not die, but if we left the mercury bichloride in the stomach more than twelve minutes, it did not make any difference what we did—wash out the stomach or give sodium thiosulfate intravenously or by mouth—the dog died

We found that the greatest factor in the prevention of death from mercury bichloride was the observation of an old principle Wash out the stomach within twelve minutes after ingestion Goldblatt called attention to the fact that if the patient vomits immediately after taking mercury bichloride, his life is usually saved

Then we decided to experiment on dogs by giving them mercury intravenously It had been previously determined by Sanson that 4 mg of mercury bichloride per kilogram given intravenously was the minimum lethal dose for a dog None ever survived this dose

If we gave the dogs 3 mg per kilogram intravenously, a few would survive even though no treatment was given So we sacrificed many dogs We gave them the sodium thiosulfate intravenously before we gave them the mercury bichloride, 4 mg per kilogram, and invariably the dogs died We gave them the sodium thiosulfate at various lengths of time after the administration of bichloride of mercury, and invariably the dogs died We gave them sodium thiosulfate by mouth and invariably the dogs died In fact, the experiment showed that sodium thiosulfate gave no protection It did not make any difference at what time or in what amount the drug was given

Then we thought that perhaps the sodium thiosulfate was causing their deaths We carried out some experiments on the toxicity of the drug and reached the point where we could give dogs 1 Gm of sodium thiosulfate per kilogram intravenously for ten to fifteen days in succession without observing any effect on the dog with the exception of a consistently lowering of the blood sugar We decided one thing definitely—that sodium thiosulfate in large doses was not toxic to dogs The effect of the mercury bichloride poisoning was interesting We made an autopsy on every dog, sectioned all the organs and found that the effect of mercury bichloride was as great on the liver as on the kidney We were inclined to believe that the tremendous rise in nonprotein nitrogen and urea, which sometimes reached

a height of 200 mg in each hundred cubic centimeters, was due as much to damage of the liver as to damage to the kidney

We went so far in our experiments on dogs that we made a permanent fistula in order to drain the gallbladder after sublethal doses of mercury had been given intravenously to see if the mercury was excreted through the bile, but at that time we did not have an accurate method by which we could determine the amount of mercury in the bile

Our experiments, which were carried on some twelve or fifteen years ago, were exactly the same as the experiments carried out by Dr Becker

We must grant then that certainly sodium thiosulfate is not a sure cure in any kind of heavy metal poisoning, but we have evidence to show that sodium thiosulfate has some sort of action in human beings that it does not have in animals, that protects them to some extent against arsenical poisoning

Now, the tests for arsenic in the urine and in the blood of human beings have not been worth anything until the last five years because of the fact that chemically pure sulfuric acid contained enough arsenic that it could be recovered from the specimen. A great deal of work has been done on spinal fluid as to the excretion of arsenic, but to my mind the results are erroneous, owing to the fact that even the so-called chemically pure substance contained traces of arsenic

We have now a sulfuric acid that is as near free of arsenic as can be, and I think that the chemical work that is going on at present is a great deal more accurate than it was before

This has been a very nice piece of work Dr Becker has done. He has delved into the matter again and has shown that as far as animals are concerned this drug offers no protection. But one thing must be remembered which is never mentioned in experimental work. The human body has a set of excretory organs, known as sweat glands, which the dog and the rabbit and the cat do not possess

DR SAMUEL GOLDBLATT, Cincinnati. I want to amplify Dr Dennie's remarks a little. It is true that we were unable to show the slightest beneficial effect from extremely large doses of sodium thiosulfate administered to dogs that had been poisoned with mercury bichloride, given either by mouth or intravenously, if they were kept under the influence of ether or other anesthetic so that they did not vomit for more than twelve minutes. However, experiments that went on with cholecystotomies and fistulas, following Dr Dennie's acquaintance with the work, were distinctly successful, although we were unable to measure the amount of mercury excreted. Dogs poisoned intravenously by twice the minimal lethal dose of mercury bichloride recovered and were re-poisoned several times, as long as the tube leading from the gallbladder to the outside was kept open. When the tube was closed, the dog began to show all the symptoms of classic mercury bichloride poisoning.

To get back to the question of the arsenicals with reference to human beings I have maintained for fifteen years that one of the prime reasons for bad results with sodium thiosulfate in the treatment of arsenical intoxication in patients was the small size of the dose. I have never administered to a human being a dose of less than 3 Gm intravenously. I have given on many occasions as high as 15 Gm intravenously. Our routine during the period that we were studying acute mercury bichloride poisoning in the wards of the Cincinnati General Hospital was to administer 10 Gm of sodium thiosulfate four times a day.

The drug when freshly prepared from an alcohol-precipitated crystal is apparently much less toxic than ordinary salt solution. The results in acute arsenical

dermatitis and in chronic arsenical dermatitis, including the arsenical fixed eruptions, when sodium thiosulfate is given in adequate doses, are quite dramatic

DR S WILLIAM BECKER, Chicago I think one of the reasons sodium thiosulfate does not protect from metallic poisoning is that the p_H of the body is not on the acid side

With regard to larger doses of sodium thiosulfate, it is known that they are perfectly safe Voegtlin and his co-workers could give rabbits up to 4 Gm per kilogram, which is a large dose, before disagreeable symptoms began In mice, another worker could give up to 3.8 Gm per kilogram before the drug proved fatal

There are two phases of the investigation that this work suggests continuance of The first is the correlation of studies on arsenic Unfortunately, practically every worker with arsenic uses a different method for the determination of arsenic content and, as Dr Dennie has just stated, the methods are changing and are becoming more reliable The only way to overcome that difficulty is to take all the methods that have been used and check them against one another and see how they compare The most logical explanation for the action of sodium thiosulfate is that of formation of sulfur in the body Dr Klauder has shown that in exfoliative dermatitis the sulfur in the skin is very low Whether in the doses given it is possible to supply enough sulfur to make up that deficit, I think is questionable and may be an argument for the large doses recommended by Dr Goldblatt

There certainly are several things about its action that are not understood, but one must admit that there is something about sodium thiosulfate therapy that helps the patients

PREVENTION OF INDUSTRIAL DERMATITIS

WITH REFERENCE TO PROTECTIVE HAND CREAMS, SOAP AND THE
HARMFUL ROLE OF SOME CLEANSING AGENTS

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ELMER R GROSS, M D

AND

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PHILADELPHIA

The important role of cleansing agents applied to the skin in the causation of industrial dermatitis has been stressed by a number of writers. It is worthy of emphasis that trade dermatitis is caused annually in an enormous number of cases not by the substances encountered at work but by the removal of these substances with methods harmful to the skin¹. Soap and water constituted a contributory factor in the production of eruptions in at least 249 of Downing's² series of 2,000 cases of cutaneous disease arising in industry. Horner³ remarked that he had observed more cases in which dermatitis was due to the improper use of cleansing agents than cases in which the dermatitis was due to contact in the occupation.

For the purpose of this study we questioned in detail all patients and other persons employed in industry concerning the manner in which they washed their hands, the kind of soap used, by whom it was furnished (employer or employee), the frequency of washing and the use of other cleansing agents, emollients and protective medicinal applications. In addition, we made surveys of factories and workshops in different industries, to obtain the aforementioned information and also to observe facilities provided for washing and measures other than mechanical employed in the prevention of industrial dermatitis.

Our observations emphasized measures in prevention of industrial dermatitis which other writers have stressed and which we shall not

From the Research Institute of Cutaneous Medicine

Read at the Sixty-Second Meeting of the American Dermatological Association, Inc., Monte-Bello, Quebec, Canada, June 3, 1939

1 Overton, S. Industrial Dermatoses. Their Causation, Recognition, Prevention, and Treatment, *Brit J Dermat* 41 255, 1929

2 Downing, J. G. Cutaneous Eruptions Among Industrial Workers. A Review of Two Thousand Claims for Compensation, *Arch Dermat & Syph* 39 12 (Jan) 1939

3 Horner, S. G. Some Observations on Industrial Dermatitis, *Lancet* 2: 233, 1934

discuss Reference is made to mechanical devices to replace manual contact, exhaust systems, closed processes, clean protective clothing, shower bath facilities, general department sanitation ("house cleaning" in the sense of the safety engineer) and hygienic practice of the worker. Such measures in the prevention of industrial dermatitis are essentially an engineering problem and are more fundamental than are the use of protective applications to the skin and the use of cleansing agents, which are concerned in this paper. These measures are especially in effect in large factories with a safety engineering department. They are frequently lacking, doubtless for financial reasons, in the smaller factory or workshop.

Not until industry is more mechanized and the worker and others concerned are better educated (in the manner later discussed) will the measures concerned in this paper become an anachronism. Our observations emphasize the need of education regarding the following important factors in the prevention of industrial dermatitis: the use and abuse of soap, the use of soap substitutes, the proper and improper use of cleansing agents other than soap, the use of emollients, the unnecessary exposure of the skin to primary irritants and to sensitizing substances, the use of a brush instead of a cloth, the use of a tool instead of the hand, the use of protective sleeves⁴ and the provision of facilities and preventive means that are simple and easily provided. The industrial physician should show greater interest in what appears to be a minor consideration: the method used by employees in his plant to cleanse their hands.

Our observations cause us to marvel at the efficacy of the human skin in resisting abuse and irritation and to express surprise that there is not a greater incidence of industrial dermatitis than now prevails.

Safety engineers with whom we conferred had a proper concept of the problems involved in the prevention of industrial dermatitis. The real difficulty is the education of the worker himself and of others concerned. In this connection, Downing⁵ noted a decrease of nearly 75 per cent in the incidence of industrial dermatitis in one plant after a recent lecture.

PROTECTIVE MEDICINAL APPLICATIONS

In the absence of mechanical measures of protection and when gloves are not worn, protective applications to the skin are to some degree effective. There are disadvantages to the wearing of gloves, they are usually not worn unless there is exposure to powerful cutaneous

4 We refer to the need of a greater choice of material and design than is, according to our experience, now available. We refer to the use of such articles as fingerless gloves or a glove and protective sleeve in one piece and to the use of materials for protective sleeves and gloves that are light yet durable (for instance, airplane cloth, oiled silk, cellophane and phofilm).

5 Downing, J. G. *The Skin and Industry*, *Indust Med* 1 19, 1932.

irritants. Circumstances in which protective applications are indicated embrace different occupations, in which the work is of a dry, wet or dusty character or entails exposure to primary irritants or sensitizing substances.

The application of a simple agent, such as hydrous wool fat, glycerin, a bland oil, grease, cream or paste, or even talc, may afford some degree of protection and for this purpose have been recommended by many writers. We believe, however, that the protective action of such simple agents can be improved by the addition of other ingredients or by a combination of different agents in appropriate vehicles.

Curschmann⁶ advised equal parts of zinc oxide and olive oil or of eucerin (oxycholesterol) anhydrate and glycerin. Hopf⁷ recommended chinisol (potassium hydroxyquinoline sulfonate). Schultze,⁸ referring to Germany, stated that there are a great number of protective creams commercially available, some of which are especially prescribed for certain industries.⁹ Attempts have been made to employ preparations that "tan the living skin." Such a preparation (known as cutigen, a mixture of tannins obtained from oak bark and other vegetable matter) has been proposed by Haustein and Jager¹⁰ as a protective application.

Some writers recommend the use of a protective ointment, cream or paste without specifying its nature. Few formulas have been published. The following have been recommended:

| By James ¹¹ | Per Cent |
|------------------------|----------|
| Ivory soap flakes | 7.48 |
| Glycerin | 26.40 |
| Sodium silicate | 24.20 |
| Tragacanth | 0.21 |
| Oil of Lemon | 0.16 |
| Water | 41.60 |

6 Curschmann, F. Vorkommen, Entstehung und Verhütung beruflicher Hauterkrankungen, *Arch f Dermat u Syph* **173**:222, 1935.

7 Hopf, G. Ueber die Begutachtung von Gewerbedermatosen, *Dermat Wchnschr* **107** 1129, 1938.

8 Schultze, W. Bisherige Arbeiten auf dem Gebiet der Hautreinigung mit Anregungen für die weitere Arbeit, *Zentralbl f Gewerbehyg* **15** 81, 1938.

9 The foreign preparations lupocid (salicylic acid, resorcinol, carvacrol [methyl-isopropylphenol, $\text{CH}_3\text{C}_6\text{H}_4\text{OH}$ C_3H_7], chlorocarvacrol, naphthol, bismuth and magnesium silicate in petrolatum) and borolan (yellow wax, honey, boric acid, olive oil in a petrolatum and hydrous wool fat base) were recommended as protective as well as medicinal applications. According to Finkenrath (*Die Wirksamkeit einiger Schutz- und Heilmittel gegen Berufsektzeme*. I. Lupocid und Borolan, *Zentralbl f Gewerbehyg* **14**:206, 1937), these preparations are not efficacious as protective applications.

10 Haustein, F., and Jager, R. Die technik der Lebendgerbung, München *med Wchnschr* **81** 143-144, 1934.

11 James, A. P. R. An Aid in the Management of Occupational Contact Dermatitis (Dermatitis Venenata), *Arch Dermat & Syph* **30** 30 (July) 1934.

| <i>By Fantus</i> ¹² | | Per Cent |
|--------------------------------|--|----------|
| Zinc stearate | | 8 00 |
| White wax | | 4 00 |
| Spermaceti | | 12 00 |
| Wool fat | | 8 00 |
| White petrolatum | | 48 00 |
| Rose water | | 20 00 |
| Oil of rose | | 0 02 |

| <i>By Collis</i> ¹³ | | |
|--------------------------------------|-----------------------|--|
| "Mineral lard" (probably petrolatum) | 3 pounds (1 36 Kg) | |
| Paraffin | 6 ounces (170 1 Gm) | |
| Cyllin (a preparation of creolin) | 3 ounces (85 05 Gm) | |

A number of preparations labeled "protective" (creams, liquids, ointments and pastes) are available commercially in this country. The exact ingredients of most of them are not known. As far as we have been able to determine, the active ingredient (the substance that leaves a film on the skin) is paraffin, wax, gum, sodium silicate or casein.

Some of the commercial preparations contain soap. We regard this as undesirable. As is later discussed, one objection to soap as a detergent is its alkalinity, which interferes with the normal acid reaction of the skin.

In our study, in which we proposed different formulas, we endeavored to fulfil certain requirements. The preparation should be sufficiently adherent so that it is not easily rubbed off, and yet it should be possible to remove it without too much difficulty at the end of the work day. Objectionable features should be lacking, such as excessive greasiness, stickiness and drying effect on the skin. The ingredients should have no, or very little, sensitizing capacity. A choice of applications of a greasy, nongreasy or waterproof character should be available, as the nature of the work demands.

In selecting ingredients, we considered the following substances that when applied to the skin leave an impervious coating or film: rubber (latex), rubber compounds (pliolite, Goodyear), synthetic rubber (neoprene, DuPont, koraseal, Goodrich), various guttas, vegetable gums, glues, resins, paraffin, yellow wax (beeswax), silicic acid and its compounds, casein, agar and cellulose and its compounds. The newer plastics employed for a variety of industrial purposes (artificial resins, such as alkyd and vinyl resins), phenol formaldehyde, urea formaldehyde

¹² Fantus, B. General Technique of Medication, ed 3, Chicago, American Medical Association, 1938, p 138.

¹³ Collis, cited by Downing.⁵

and coumarone were considered but were not employed on account of their sensitizing capability

From this list we selected substances that were regarded as appropriate and compounded them alone or in combination in varying percentage in different bases¹⁴ We selected the formulas which are given in the following paragraphs and subjected them to clinical trial

Group 1—This group of substances comprised compounds of petrolatum or benzoized lard, stiffened with paraffin, yellow wax, hydrogenated cottonseed oil or synthetic wax (glyceryl monostearate^{14a}), to which was added one or more of the following substances sodium silicate, latex,¹⁵ acacia, glycerin, hydrous wool fat (lanolin) and sulfonated olive oil From this group different combinations were compounded The following ointments were selected, since they were not too greasy or too stiff

| <i>Formula 1</i> | Per Cent |
|-----------------------------|----------|
| Petrolatum | 70 0 |
| Hydrogenated cottonseed oil | 30 0 |

Formula 2

(*A modification of simple ointment U S P*)

| | |
|--|------|
| White wax ¹⁶ | 5 0 |
| Glyceryl monostearate ^{14a} | 12 5 |
| Hydrous wool fat | 5 0 |
| Sodium silicate, commercial solution | 5 0 |
| Ammonium hydroxide, 10% solution | 0 5 |
| Petrolatum | 72 5 |
| The ammonium hydroxide is incorporated to prevent precipitation of the sodium silicate | |

Formula 3

The preceding preparation is enhanced by the addition of 5 per cent (by weight) of latex, which produces a rubbery film on the skin The base is melted, latex is added during stirring, and the stirring is continued until congelation occurs

Formula 4

The following preparation has a p_H of 5.4 and is therefore recommended when there is prolonged contact of the hands with soapy water

| | Per Cent |
|--------------------------------------|----------|
| White wax | 10 0 |
| Hydrous wool fat | 5 0 |
| Glyceryl monostearate ^{14a} | 12 5 |
| Stearic acid | 2 0 |
| Petrolatum | 75 5 |

¹⁴ This phase of the work was done by Aaron Lichtnin, Ph G, who made valuable suggestions

^{14a} Glyceryl monostearate may be obtained as Xerol A (Fries Brothers)

¹⁵ Latex is the milk juice of the trees that are used to supply rubber We employed the preparation lotol Nc 957, Naugatuck Chemical Company, New York, which consists of 60 to 63 per cent concentrated latex

¹⁶ The white wax employed in this and all other formulas was white wax U S P

Formula 5

The following preparation to water-proof the skin is recommended when there is prolonged contact with water

| | Per Cent |
|------------------------------------|----------|
| White wax | 100 |
| Hydrous wool fat | 50 |
| Sulfonated olive oil ¹⁷ | 100 |
| Petrolatum | 750 |

Group 2—Formulas 6, 7 and 8 are clean nongreasy preparations that dry on the skin and do not rub off. Their use is indicated, therefore, in dry work, as a protection against dust-borne irritants or when soiling of material or objects by the protective is not desirable. Formula 6 is smeared on the skin, whereas formulas 7 and 8 are liquids and are applied by means of a brush or swab.

| | <i>Formula 6</i> | Per Cent |
|--------------------------------------|------------------|----------|
| Glyceryl monostearate ^{14a} | | 120 |
| White wax | | 120 |
| Wool fat | | 60 |
| Cholesterol | | 10 |
| Sodium silicate, commercial solution | | 50 |
| Ammonium hydroxide, 10% solution | | 05 |
| Water | | 635 |

Melt white wax, glyceryl monostearate, hydrous wool fat and cholesterol in one pot. Add sodium silicate solution and ammonium hydroxide solution to water previously heated in another pot. Stir aqueous solution into the wax mixture.

Preparations of mastic solution in acetone dry and leave a film on the skin.

| | <i>Formula 7</i> | Per Cent |
|-----------------------------------|------------------|----------|
| Ethyl cellulose | | 50 |
| Mastic | | 80 |
| Castor oil | | 10 |
| Acetone (technical) ¹⁸ | | 860 |

| | <i>Formula 8</i> | Per Cent |
|--|------------------|-----------|
| Polyvinyl acetal resin (Monsanto Chemical Co.) | | 5 to 100 |
| Castor oil | | 10 |
| Acetone (technical) ¹⁸ | | 89 to 940 |

In both these formulas use whole mastic, not the powder. Allow the mastic to stand in acetone overnight. A residue remains. Use supernatant fluid as a solvent for the other ingredients.

In formula 7 ethyl cellulose ¹⁹ was regarded as more desirable than pyroxylin or myrrh, the use of which was studied. In formula 8 an alkyd resin (rezyl 19, American Cyanamid and Chemical Co.) was not superior to the vinyl resin employed. Neither formula is entirely

¹⁷ The type known commercially as 75 per cent

¹⁸ The more expensive, chemically pure grade could also be used

¹⁹ Dr. James H. Sterner, of the medical department of the Eastman Kodak Company, stated that from extensive experience with workmen exposed to ethyl cellulose, this chemical has a low sensitizing capability.

removed by washing, but the residue is readily removed by acetone. If the latter is employed, an emollient should be used, especially in winter.

Group 3—Another type of protective is a thick paste that leaves a water-proof, impervious covering

| | <i>Formula 9</i> | Per Cent |
|------------------|------------------|----------|
| Zinc oxide | | 25 0 |
| Kaolin | | 25 0 |
| White petrolatum | | 50 0 |

This preparation affords more protection than any of the other formulas, and it also water-proofs the skin. Its disadvantages are that it is somewhat sticky and it soils objects in contact with it, since it rubs off to some degree. It is therefore appropriate only in certain work

OTHER PROTECTIVE APPLICATIONS

Hydrous wool fat (lanolin) has been effective in preventing cancer in experiments in which carcinogenic agents were applied. This fact is in keeping with the observation that animal and vegetable oils do not act as carcinogenic agents and that the natural cutaneous fat is an important factor in the prevention of experimental cancer.

It was shown by the Tworts²⁰ in experimental studies that equal parts of olive oil and wool fat (anhydrous) made the most efficacious ointment for protection from the carcinogenic action of mineral oils and tars. It was recommended that this mixture be applied to the exposed skin of workers handling carcinogenic oils, tars and most of their products before commencing work, and that at the end of the work day the soiled skin be thoroughly washed with soap and water and that hydrous wool fat again be applied.

In addition to personal cleanliness and frequent washing of the exposed parts, different applications have been recommended for the prevention of dermatoses in those who work with petroleum and lubricating oils. Scott²¹ recommended crude castor oil, since it is impervious to paraffin. Downing² advised the application of greaseless creams and of equal parts of boric acid solution and alcohol before and after work. Dusting the arms with equal parts of starch and powdered zinc oxide has been suggested.²² In Bridge's²³ experience, washing

²⁰ Twort, C. C., and Twort, J. M. The Utility of Lanolin as a Protective Measure Against Mineral Oil and Tar Dermatitis and Cancer, *J. Hyg.* **35** 130, 1935, On Prevention of Mineral Oil and Tar Dermatitis and Cancer, *Lancet* **1**:286, 1934.

²¹ Scott, A. The Occupational Dermatoses of the Paraffin Workers in Scottish Shale Oils, *Brit. M. J.* **2**:381, 1922.

²² Memorandum on Cutting Lubricants and on Skin Diseases Produced by Lubricants, Bulletin 2, Department of Scientific and Industrial Research, London,

with dilute solution of sodium hypochlorite before and after work was an effective preventive measure, which was doubtless directed against some infectious agent in the oil, although this cause of oil dermatosis is questionable. McConnell²⁴ advocated the application of hydrous wool fat or equal parts of hydrous wool fat and castor oil. In Hausser's²⁵ experience the best results were obtained with the application of glycerin before work and after work a solution containing sodium bicarbonate 20 Gm, glycerin 5 cc, chlorine 3 Gm and water 100 cc.

Shepard and Krall²⁶ advised the application of an alkaline solution, such as sodium bicarbonate, to the arms of persons working with rubber in order to neutralize the acid of the sweat and thus to prevent dermatitis from methenamine (hexamethylene tetramine). This accelerator, however, is being replaced by less dangerous ones.

Horner³ recommended that cottonseed oil be applied to the hands before exposure to paint and printing ink in order to facilitate their removal from the skin. For a similar purpose McConnell²⁷ advised that equal parts of hydrous wool fat and olive oil be applied to the hands and arms of printers before they commence work. He concluded from his studies that the mechanical removal of ink by brush is responsible for the initiation of dermatitis among printers, and not adulterants of oil of turpentine.

We advise workmen whose hands become soiled to apply before commencing work olive oil, neat's foot oil, hydrous wool fat or linseed oil. Such application facilitates the removal of dirt, grease and grime, especially if one of these oils is applied again to the soiled parts and removed with a clean cloth before washing with soap and water.

In prevention of dermatitis from wood-preserving materials in which coal tar distillate, water gas tar and zinc chloride are the substances regarded as the causative agents, the application of hydrous wool fat containing 10 per cent sodium bicarbonate has been recommended.²⁸

1918, p. 8, cited by Downing, J. G., and Welch, C. E. *New England J. Med.* **206** 666 (March 31) 1932.

23 Bridge, J. C. *Occupational Diseases of the Skin*, Brit. M. J. **2** 324, 1933.

24 McConnell, W. J. *Dermatoses Following the Use of Cutting Oils and Lubricating Compounds*, Pub. Health Rep. **37** 1773, 1922.

25 Hausser, G. *Les dermatoses professionnelles dues aux huiles de graissage*, Presse méd. **46** 295, 1938.

26 Shepard, N. A., and Krall, S. *Poisons in the Rubber Industry. The Rash Produced by Hexamethylene-Tetramine and a Means of Prevention*, J. Indust. Hyg. **2** 33, 1920.

27 McConnell, W. J. *Industrial Dermatitis Among Printers*, Pub. Health Rep. **36** 979, 1921.

28 *Dermatitis from Wood Preserving Materials, Queries and Minor Notes*, J. A. M. A. **97** 799 (Sept. 12) 1931.

The application to the hands of pine tar as a protection (?) against lime is a traditional remedy (without scientific basis) used by workers in tanneries (case 11)

A solution of sodium bisulfite (NaHSO_3) as a reducing agent is an effective remedy. Its use is especially indicated before and after exposure to chromic acid and chrome compounds, since it reduces them to the non-irritating chromous state. In this regard, White²⁹ advised that a concentrated solution be allowed to dry on the skin before exposure and that a strong solution be used as a wash after exposure. He recommended as a general rule that in all industries involving exposure to chemicals, dyes, drugs, coloring materials, irritating dusts or fluids the hands be swilled in a solution of sodium bisulfite preparatory to the ordinary washing and also after using the commonly employed mixture of anhydrous sodium carbonate (soda ash) and calcium hypochlorite (hypochlorite of lime) to remove stains caused by dyes.

HARMFUL AND HARMLESS METHODS OF CLEANSING THE SKIN

Neutralizing Solutions and Applications to be Used After Work—

A common practice among industrial workers is to use on the hands, for removing dye, paint or other stains, solvents or chemicals that are used in their work (cases 4, 5 and 8). Such cleansing agents are either primary cutaneous irritants or sensitizing or defatting substances, and those usually employed are turpentine, alcohol, wood alcohol, naphtha, acetone, amyl acetate, gasoline, kerosene, benzine, calcium hypochlorite and various acids and alkalis. Workers whose occupations require the use of paint, varnish, stain or lacquers invariably use turpentine, paint thinners or a solution of sodium carbonate. Machinists use kerosene, automobile mechanics, gasoline. Printers, type setters and lithographers employ type wash, turpentine or kerosene. The practice in dye houses or where coloring material is handled is to remove the dye or stain with a bleaching solution—calcium hypochlorite or sodium hypochlorite. The following are commonly employed trade formulas: one pound (0.45 Kg) each of anhydrous sodium carbonate (soda ash) and calcium hypochlorite to 3 gallons (11.36 liters) of water (this amount or less of sodium carbonate alone suffices), and for acid dyes, 63 Gm of sodium hypochlorite, 5 Gm of sodium chloride and 15 Gm of sodium hydroxide to 1 liter of water. If these methods are employed, solutions of minimum strength should be used, followed by rinsing in running water and immersion of the hands or forearms in a solution of sodium bisulfite (NaHSO_3).

²⁹ White, R. P. *The Dermatergoses, or Occupational Affections of the Skin*, ed. 4, London, H. K. Lewis & Co., Ltd, 1934, p. 339.

A harmless yet efficacious method of removing dye or other stain is the free application of a 10 to 30 per cent solution of sodium bisulfite (NaHSO_3). If this does not suffice, it should be used after the application of a 1 2,000 to 1 4,000 solution of potassium permanganate. If sodium bisulfite solution is allowed to dry on the skin before beginning work stains are more easily removed.

To remove such substances as paint, oils and grease, a 1 to 2 per cent solution of a commercial solution of sodium silicate or, what is superior to this, a 0.5 to 1 per cent solution of sodium metasilicate can be employed. The latter chemical should be considered in the removal of any foreign substance from the skin and as a general cleanser.

During or after exposure of the hands to acids or alkalis the following noninjurious solutions should be employed: for acids, a saturated solution of either sodium bicarbonate or sodium borate ($\text{Na}_2\text{B}_4\text{O}_7$), and for alkalis, a 3 to 4 per cent solution of acetic acid or a saturated solution of boric acid. A good method of removing from the skin stains caused by trinitrophenol (picric acid) is the application of a paste of magnesium carbonate.³⁰

In the prevention of "photographer's dermatitis" the British Chief Medical Inspector of Factories in his report for 1929 advised that after exposure to metol (a proprietary photographic developer, methylaminocresol sulfate) the hands should be immersed in a weak solution of a mineral acid and that in subsequent washing no soap containing a free alkali should be employed. In an attempt to prevent dermatitis from contact with developing solutions at the Eastman Kodak Company, the Medical Director³¹ of the Eastman Park Works informed us that rinsing in a 1 to 3 per cent solution of acetic acid is practiced after exposure, followed by rinsing with a great deal of water.

The application of bland oils (olive, cottonseed and linseed oil and liquid petrolatum) has long been advised in order to facilitate the removal of dirt prior to the use of soap and water.³² The addition of one of these oils or of liquid soap to sawdust has been advised. Sulfonated oils, either olive or neat's foot, mixed with an equal part of liquid petrolatum are preferable to the aforementioned ones.

The use of an abrasive soap or of a hand brush is mechanically irritating and should therefore be avoided.

We advise the following formula as a substitute for the popular mechanic abrasive soaps. Equal parts of sulfonated neat's foot oil and liquid petrolatum containing 25 per cent gelatin (formula 12) are

30 Dermatitis from Trinitrophenol, *Queries and Minor Notes*, J A M A 95 1284 (Oct 25) 1930

31 Slater, B J. Personal communication to the authors

32 Emulsified preparations dispensed as cosmetics have been exploited as cleansing agents. These, however, have no place as cleansing agents in industry.

added to white granulated corn meal³³ in the proportion of 1½ parts, by weight, of corn meal and 1 part, by weight, of the oil mixture. To prevent growth of mold or bacteria a 0.5 per cent solution of chlorobutanol is added. Corn meal of a wide variety of particle sizes is obtainable. White granulated meal was selected, since the particle size was adapted for abrasive purposes. The corn meal and oil mixture has the appearance of wet sand. The p_H of the mixture is about 5. As a detergent it is used with water in the same manner as is soap. The addition of 1 to 2 per cent sodium hexametaphosphate (p_H 6) or 2 per cent sodium metasilicate enhances the preparation when employed to cleanse particularly dirty or greasy hands. With the addition of 2 per cent sodium metasilicate the p_H of the mixture was 7.1. It is not desirable to make the mixture alkaline by the addition of mineral detergents. We doubt the necessity of this, since in our observation the mixture alone cleaned soiled hands of workmen as effectively as does any abrasive soap. After its use soap is not necessary. The mixture acts not only as a detergent but as an emollient.

Another substitute, although less desirable since it is alkaline, is the following. To cleanse soiled, especially oily and greasy, hands, they are first immersed in a 1 per cent solution or less of sodium metasilicate and then washed with a mixture of equal parts, by weight, of flaked (chip) soap and granulated corn meal.

It is advisable that sulfur soap rather than any other soap be used by workmen exposed to lead.

In our survey less than 10 per cent of the workmen apply an emollient to the hands in winter at the end of the work day. For this purpose we advise equal parts of hydrous wool fat and olive oil, cottonseed oil or neat's foot oil.

SOAP AS A DETERGENT

The custom among workmen is to use the same soap for washing their hands that is used for industrial or for purposes other than toilet in their place of employment (cases 1, 2, 6 and 7). Usually such soaps are not appropriate for toilet purposes.

Mechanic Soap—In our observations the most frequently employed soap by workmen whose hands become soiled is a well known abrasive (grit) cake soap (p_H 8.2) or a well known abrasive soap paste (p_H 10).

We were able to find, and gave consideration to, forty-four commercially available mechanic soaps. Of these forty-four, seventeen are abrasive pastes (hand grit paste soap), fifteen are gritty powders (hand scouring powder), four are abrasive (grit) cake soaps, three are liquid,

³³ The manufacturer informed us that no bleaching agent or other ingredient is contained in corn meal. In preparing the corn for the production of corn meal, only the germ and part of the bran are removed.

two are ointment-like and one is a soft soap. The abrasive agent in these soaps is probably inorganic punice, silicon dioxide (silica, silex) or sand. There is at least one exception, in which the abrasive agent is corn meal. The hydrogen ion concentrations of 1 per cent aqueous solutions of these soaps range from 8.2 to 10, with one exception, in which the p_H is 3 and which is therefore not soap in the sense of a saponified vegetable or animal oil.

Federal specifications³⁴ for a hand grit soap allow free alkali 0.1 per cent, alkaline salts (calculated as sodium carbonate) not to exceed 1 per cent and insoluble siliceous material not less than 25 per cent or more than 40 per cent, for a hand grit paste soap and hand scouring powder, sodium carbonate not to exceed 2 per cent, free alkali 0.02 per cent, anhydrous soap not less than 8 per cent or more than 16 per cent and insoluble siliceous material not less than 25 per cent or more than 50 per cent.

Mechanic soaps usually contain sodium silicate in large quantities, as much as 25 per cent, others contain sodium sesquicarbonate, sodium tetraborate, trisodium phosphate or sodium carbonate.

Most writers advise against the use of abrasive (grit) soaps. Until another equally effective and quick method is offered and workmen are educated in regard to it, abrasive (grit) soaps will continue to be popular. We believe that the aforementioned sulfonated oil and corn meal mixture is a good substitute for abrasive soaps.

In such instances in our observations in which the employer provided soap for the employees it was not apparent to us that any discrimination was used in selecting the soap. Most frequently a liquid soap was provided.³⁵ Liquid soaps are usually high in coconut oil content. This is an undesirable feature. Lay persons are not in a position to know what constitutes a good soap, and unbiased information is not easily obtained.³⁶

Toilet Soap—In prevention of industrial dermatitis some writers recommend "a neutral soap," "a soap not too strongly alkaline" or "a good toilet soap." What is a good toilet soap? Federal specifications

34 Federal specifications for soaps quoted in this paper are those of the United States Bureau of Standards, Department of Commerce, and were supplied (from catalog) by the Superintendent of Documents, Government Printing Office, Washington, D. C. The specifications apply only to soap sold to the Government and not to any soap commercially available.

35 The fact that liquid soap, in contrast to cake soap, cannot be taken away from the place of employment is an important consideration.

36 One exception is the information presented by Consumer's Research, a bureau organized on a noncommercial basis to provide unbiased information and counsel on goods bought by the ultimate consumer. Particular reference is made to the following volume: Phillips, M. C. *Skin Deep*, New York, The Vanguard Press, 1934.

for a good, commercially made soap for toilet use are that it should be as free as possible from water, lather freely with cold soft water, be free from rosin, sugar and other foreign matter and contain not more than 0.1 per cent free alkali. The specifications allow as much as 15 per cent of the net weight to be water.³⁷

Coconut oil, the chief oil or fat ingredient in most toilet soaps,³⁸ is generally regarded as irritating to most skins. This prompts some manufacturers to keep the percentage of coconut oil lower than 20 per cent of the oil used in the manufacture of toilet soap. Consumers Research has advised that coconut oil should comprise not more than 20 per cent of the oil in toilet soap. Weber³⁹ advised the use of not more than 10 per cent of coconut oil. The formulas he published of the perfect toilet soap comprised, in addition to coconut oil, slightly hardened oil,⁴⁰ palm oil, castor oil and olive oil.

Blank⁴¹ suggested that the saturated fatty acids of lower molecular weight (caproic, capric and caprylic) contained in coconut oil constitute its irritating agent, since these fatty acids are primary cutaneous irritants, and also that fatty acids in soap, in relation to the hydrogen ion concentration, are responsible for the irritating action of soap. He performed patch tests with fatty acids in conjunction with a buffer solution to duplicate the increase in the p_H of the skin (6 to 7.5) which occurs after washing with soap. He observed that on skin of a p_H higher than that of normal skin the fatty acids of higher molecular weight produced irritation, whereas they did not irritate the normal skin. Not only does the irritating quality of the fatty acids decrease with an increase in the molecular weight, but also the amount of alkali which must be added before a fatty acid becomes an irritant increases with the increase in the molecular weight of the fatty acid. He stated that a soap to be nonirritating should contain no fatty acid which will be irritating to the "alkalinized" skin and certainly no fatty acid which is itself an irritant to skin with a normal p_H . Such soap should be made only from palmitic and stearic acids.

37 The relative economy of soaps is measured by the cost per pound of dry soap.

38 An exception is soap in which pure olive oil is the sole oily or fatty ingredient. The term castile formerly implied this. It no longer does, since judicial verdict permits the use of the word castile without this specification.

39 Weber, K. L. *Die vollkommene toiletten Seife, Ole, Fette Wachse Seife, Kosmetik* 5:1, 1937.

40 The nature of the hardened oil is not stated. It doubtless refers to the hydrogenation of liquid oils which stiffens (hardens) them. Such hardened oil is usually added to the natural oil.

41 Blank, I. H. *Action of Soap on Skin*, *Arch. Dermat. & Syph.* 39:811 (May) 1939.

Neutral Soap—A “neutral soap” is one in the manufacture of which the amounts of alkali and of fatty acids are in exact molecular proportion, so that the finished product contains no free alkali or free fatty acid. The word “neutral” does not refer to the compound soap, which is not neutral in the chemical sense. Since soap is the salt of a weak acid (fatty) and a strong alkali (sodium or potassium hydroxide), it is, in accordance with chemical laws, alkaline. It is difficult to manufacture a “neutral” soap. Indeed, such soap is more of theoretic than of practical importance.

Concerning a “neutral soap,” Bleyberg and Lettner⁴² concluded that the differences in actual alkalinity of solutions of different soaps at the same temperature, as well as of the same soaps at different temperatures (20 to 90 C) or concentrations, were many times greater than the differences in alkalinity through the presence in the soap of a few tenths per cent of free alkali. Thus the stringent technical requirements of a minimum amount of free alkali in soaps appears unfounded. It would be better to fix the $p(\text{OH})$ concentration instead.

All soaps, whether neutral, superfatted⁴³ or containing a minimum amount of free alkali, hydrolyze in aqueous solution and are always alkaline. The alkali of hydrolysis is much greater than the amount of free alkali in the soap. Too much emphasis, therefore, need not be placed on neutral soaps or on a minimum amount of alkali as an index of good soap. We determined the p_{H} of a 1 per cent aqueous solution (with distilled water) of thirty-six toilet soaps. The range was from 9 to 11.

A number of investigators have shown that the hydrogen ion concentration of the skin is increased after the use of soap. This is attributed to absorption of alkali by keratin. The return of an acid cutaneous reaction usually occurs after several hours. It is this interference with the protective “acid mantle” of the skin that constitutes, with the defatting action, the chief objection to soap.

The “alkalization” of the skin after the use of soap suggests the use of a weak acid solution, such as 1 to 3 per cent acetic acid, as a

42 Bleyberg, W, and Lettner, H. Die Alkalität verdünnter wässriger Seifenlösungen und ihre Beeinflussung durch Zusätze freien Alkalis, *Chem Umschau d Geb d Fette, Oele, Wachse Harze* 39 241, 1932.

43 “In order to guard against the presence of free caustic soda [sodium hydroxide] in the finished soap, some makers add olive oil or (and) wool wax [wool fat], on the assumption that the caustic soda will combine with them to form neutral soap. These soaps are known as “superfatted soaps” (Lewkowitsch, J I. *Chemical Technology and Analysis of Oils, Fats and Waxes*, ed 6, revised by G H Warburton, London, Macmillan & Co, 1923). Superfating agents have little influence after hydrolysis of soap. We believe that superfatted soap has been unduly emphasized as a toilet soap.

buffer application, especially after prolonged contact with soap and water. In this regard, Jones, Murray and Ivy⁴⁴ suggested the use of a 1 per cent solution of sodium hexametaphosphate,⁴⁵ a salt of one of the polymers of metaphosphoric acid which has the property of forming a soluble nonionized complex with the alkaline earths. In solution this salt has a p_H of 6 and can buffer the skin at this acidity against a large amount of alkali.

Mangrané⁴⁶ and also Lustig and Schmerda⁴⁷ stated the belief that the degree of hydrolysis of soap is important in relation to its mildness. The degree of hydrolysis depends on the type of fatty acid and also on the alkali. Soaps with slight hydrolysis, such as those made with coconut oil and castor oil and not easily soluble in water, exert a greater defatting action, since the skin comes in contact with larger amounts of soap. Mangrané⁴⁶ advised that pure coconut oil soaps should be used only by persons with an oily skin. Potassium soaps usually hydrolyze more than sodium soaps. This would therefore suggest that shaving soaps are less irritating than toilet soaps. Indeed, it is the consensus that shaving soaps exert a milder action on the skin than toilet soaps.

Lustig and Schmerda⁴⁷ determined the hydrogen ion concentration and fatty acid and sodium contents of various soap solutions in order to ascertain the degree of hydrolysis. It was observed that sodium stearate and sodium palmate hydrolyze strongly and that their solutions are strongly alkaline to phenolphthalein. With increasing concentration of the soap, hydrolysis became less. It was lower also when the molecular weight of the saturated acids was low or when the acids were unsaturated. Hydrolysis was also less if the fatty acids present were of several kinds. The addition of an unsaturated acid to stearic acid diminished the solubility of the unsaturated fatty acid and increased that of the saturated fatty acid.

Kroper⁴⁸ stated the belief that an osmotic phenomenon between soap fluid and the skin is a factor in the irritating action of soap. He studied the dialysis of potassium soaps with different fatty acids,

44 Jones, K. K., Murray, D. E., and Ivy, A. C. Sodium Hexametaphosphate Its Use for Certain Industrial Dermatoses, *Indust Med* **6** 459, 1937.

45 Sodium metaphosphate products are marketed by Calgan, Inc., Pittsburgh.

46 Mangrané, D. Substitución del radical potásico por el sódico y vice-versa en los jabones alcalinos, *Soc. españ. de fis. y quim.* **32** 893, 1934, cited by Pfaff, K. Aus dem Notizbuch des Seifentechnikers, *Riechstoffindustrie u. Kosmetik* **10** 200, 1935.

47 Lustig, B., and Schmerda, F. Ueber die Löslichkeit der Natriumseifen. Ein Beitrag zur Pharmakologie der Seifenwirkung, *Dermat. Wchnschr.* **104** 607, 1937.

48 Kroper, H. Ueber das Verhalten der Lösungen von Seifen und Netzmitteln an halbdurchlässigen Membranen, *Dermat. Wchnschr.* **106** 381, 1938.

employing a semipermeable membrane. It was observed that hydrolysis and dialysis were in inverse ratio—the more limited the hydrolysis, the greater the dialysis. One of his specifications of a good detergent is that it should have a low dialysis index.

Lewkowitsch⁴⁹ stated that the best class of toilet soaps contain as a rule 80 per cent fatty acids. The range in cheap toilet soaps is down to less than 40 per cent. For household purposes all qualities are made, from genuine soap containing 63 per cent fatty acids down through all gradations of carbonated, silicated, "filled" and "run" soaps to "scouring" soaps, which may contain only 10 per cent of fatty acids.

The following soaps are at times employed by workmen. Of these, soap powder is the most harmful.

Scouring Soaps—These are prepared from coconut oil, to which may be added kitchen grease, saponified with sodium hydroxide (caustic soda). Sodium silicate and anhydrous sodium carbonate (soda ash) are additional ingredients, and colloidal clay or fullers' earth are sometimes added. For abrasive purposes silicon dioxide (silica, silex) powder is incorporated. Federal specifications for a grit cake (scouring) soap allow 0.1 per cent free alkali (calculated as hydroxide) and 1 per cent alkaline salts (total alkalinity of matter insoluble in alcohol) calculated as sodium carbonate, with the insoluble siliceous material not less than 88 per cent or more than 93 per cent.

*Soap Powder and Washing Powder*⁵⁰—Soap powder is a mixture of hard soap and sodium carbonate and frequently contains sodium silicate, sodium borate (borax), trisodium phosphate or other builders. Some contain a bleaching agent. The soap in some is made of cottonseed oil. Soap powders usually contain 15 to 20 per cent soap, as much as 55 per cent sodium carbonate and 10 per cent water. Federal specifications require not less than 15 per cent soap and not less than 30 per cent sodium carbonate. Some of the more recent soap powders contain more soap, as much as 60 per cent, and 30 per cent or less of mineral detergents.

Laundry or Household Soaps—Depending on the grade, these soaps are made of mixed fatty oils (coconut, palm kernel, tallow, cottonseed oil), hydrogenated oils or fatty material of low quality, such as kitchen or packing house grease and bone fat, which are fatty acids of low molecular weight. Sodium carbonate or sodium borate (borax) and

49 Lewkowitsch, J. I. *Chemical Technology and Analysis of Oils, Fats, and Waxes*, ed. 6, revised by G. H. Warburton, London, Macmillan & Co., 1923, vol. 3, p. 352.

50 Soap powder should be distinguished from "powdered soap," which includes soap chips, soap flakes, granular soaps and soap beads also employed for household uses.

sodium silicate up to about 15 per cent are used in yellow bar soaps. Federal specifications for the ordinary grade allow up to 0.5 per cent free alkali, with not less than 2 per cent or more than 10 per cent alkaline salts.

Soap Chips or Flakes—This class contains more soap (80 per cent or more) and less alkaline salts than any of the aforementioned soaps. Federal specifications allow 15 per cent water and 3 per cent alkaline salts.

Ingredients of Soap—"FILLERS"—"In soap making by the word 'filling' is understood the art of producing cheaper soaps by the mechanical addition of cheaper substances"⁵¹ The number of substances which are now incorporated in soaps so as to impart to them either some actual or assumed valuable property is legion.

In the opinion of Lewkowitsch⁵² soaps containing less than 50 per cent of fatty acids should be looked on as "adulterated," whether the fillings have detergent properties or not, unless the admixture be declared openly.

It is difficult to define what really constitutes an adulteration of soap. This has been a matter of controversy in trade and in judicial circles, particularly regarding sodium silicate. To serve a purpose regarded desirable by some manufacturers a variety of fillers may be added. For example, alcohol, castor oil, or glycerin and sugar are used for making transparent soaps.

FILLING MATERIALS—These consist essentially of salts soluble in water, such as sodium and/or potassium chloride and sodium and/or potassium sulfate, alkali carbonates, silicates; mineral substances, such as talc, titanium and/or zinc oxide, sodium and/or barium sulfate, silicious materials, and organic substances, such as potato starch.

SILICATES OF SODIUM⁵³—Sodium silicate is an important ingredient of soap. In addition to its presence in household and mechanic soaps, as already discussed, some toilet soaps contain 1 to 4 per cent. Soaps made from certain fat stocks become rancid on exposure to air. The presence of silicate prevents this. In addition it is added to soap to whiten and harden it, to produce a firm, smooth texture and to increase the lather, emulsifying power and detergency. It is therefore maintained that silicate is a "builder" and not a "filler."

51 Dete, C. *Manual of Toilet Soapmaking*, ed. 2, translated by A. H. J. Keane, London, Scott, Greenwood & Son, 1920, p. 143.

52 Lewkowitsch,⁴⁹ p. 344.

53 Richardson, A. S. *The Action of Sodium Silicate When Used in Soap*, *Indust. & Engin. Chem.* **15**:241, 1923. Stericker, W. *The Value of Silicate of Soda as a Detergent*, *ibid.* **15**:244, 1923. Vail, J. G. *The How and Why of Silicate of Soda*, *Soap* **4**:18, 1928. *Soluble Silicates in Industry*, American Chemical Society Monograph, New York, Reinhold Publishing Company, 1928.

In the manufacture of soap, the 40 per cent commercial solution of sodium silicate is employed. It is not a definite chemical compound but a combination of different relative amounts of sodium monoxide and silicon dioxide (silica). We noted by patch tests that the commercial solution is not a primary cutaneous irritant.

Sodium metasilicate⁵⁴ (more properly sodium metasilicate pentahydrate, $\text{Na}_2\text{SiO}_3 \cdot 5\text{H}_2\text{O}$) and sodium sesquisilicate⁵⁵ ($3\text{Na}_2\text{O} \cdot 2\text{SiO}_2 \cdot 11\text{H}_2\text{O}$, or the pentahydrate of trisodium orthosilicate) are definite chemical compounds that have a power for wetting surfaces and emulsifying oils and are deflocculating agents. They are therefore detergents and are used for a variety of industrial purposes (in laundries and in washing bottles, dishes, metals, machinery and garage floors) alone or with soap.

A 1 to 2 per cent solution of a commercial solution of sodium silicate or a 1 per cent solution or less of sodium metasilicate placed in the palms and rinsed with water serves as a detergent.

We performed patch tests on normal persons with 2, 4 and 6 per cent solutions of sodium metasilicate. Negative results were obtained⁵⁶. A 25 per cent solution produced a mild erythema only on some persons.

ALLERGENIC ACTION—We do not believe that the compound soap is allergenic. Excluding medicated soap, the notable allergenic ingredients of soap are dyes, perfumes, essential oils and possibly the salts of rosin acids⁵⁷.

Cutaneous Irritants—The factor causing soap to be a primary cutaneous irritant may be the fatty acid, as suggested by the work of Blank⁴¹. On the other hand, Lewkowitsch and Warburton⁵⁸ stated that the quantities of free fatty acid that are liberated after hydrolysis of soap

54 Sold under the trade name of metso (Philadelphia Quartz Co., Philadelphia)

55 Metso 99

56 Although sensitization to silicates of sodium has been reported (Blaisdell, J. H. *Medicolegal Complications in Dermatology Caused by Massachusetts Workmen's Compensation Act*, Arch Dermat & Syph 39 77 [Jan] 1939), it is apparently rare.

57 Rosin is the resinous matter remaining after distillation of the volatile oil from turpentine. It is used as a cheap substitute for fatty matter in the manufacture of soap, since the alkali salts of rosin acids have detergent properties. Rosin imparts a yellow color to soap and is used in the manufacture of yellow laundry soap bars.

58 "When dissolved in water soap suffers hydrolysis to an extent dependent on the dilution, resulting in the precipitation of acid soaps (e. g. sodium hydrogen palmitate) and the liberation of a small amount of free alkali and infinitesimal quantities of free fatty acid" (Lewkowitsch, E., and Warburton, G. H. *Soap*, in *Encyclopaedia Britannica*, ed 14, New York, Encyclopaedia Britannica, Inc., 1937, vol 20, p 858).

are infinitesimal. In spite of the statements in the literature to the contrary, we do not believe that the alkalinity per se acts as a cutaneous irritant.

Cake soap (laundry, household or mechanic) is not sufficiently soluble to allow the alkaline salts contained in it (fillers and builders) or indeed any other ingredient in sufficient concentration in the soap solution to act as a primary cutaneous irritant. Soap used for washing hands is employed in solution of 1 per cent or less and in not much greater percentage for household purposes.

The foregoing statement applies to all soap in which the alkaline salts are added after the fats and alkali have been combined. Alkaline salts mixed with the finished soap to constitute soap powder or mixed with abrasive material to constitute gritty powders (hand scouring powder) for mechanic use may be more likely to act as cutaneous irritants by reason of their ready solubility.

To our knowledge, the concentration, if any, of all the alkaline salt detergents used as fillers or builders that acts as a cutaneous irritant has not been determined. We observed by patch tests that the normal skin did not react to a 35 per cent solution (saturated at room temperature) of anhydrous sodium carbonate. The results of patch tests with the other alkaline salt detergents thus far suggest that even in saturated solution they are not primary cutaneous irritants. The role of alkaline salt detergents as cutaneous irritants, we believe, is not inherent to their employed strength but concerns prolonged exposure of the skin to them, whereby they become irritants either because the threshold of irritability of the skin is lowered (toxic hypersensitivity in the sense of Burckhardt) or because the skin becomes allergic to them.

In Burckhardt's⁵⁹ studies of the sensitivity of the skin to alkali, its capability to neutralize alkali and the eczema due to alkali, notably that of masons, he concluded that decreased resistance of the skin to alkali (toxic hypersensitivity) is an important etiologic factor in this form of eczema rather than an allergic hypersensitivity. Toxic hypersensitivity concerned impaired function of the skin to neutralize alkali.

Burckhardt's studies suggest that dermatitis from soap in its broadest meaning and from alkaline cleansers other than soap, as herein discussed, concerns a toxic hypersensitivity rather than an allergic hypersensitivity. His studies emphasize the fact that alkaline detergents are not ideal. They should be used sparingly or in minimum concentration. The importance of applying buffer applications to the skin after their use, as previously discussed, becomes apparent.

59 Burckhardt, W. Beiträge zur Ekzemfrage. Die Rolle des Alkali in den Pathogenese des Ekzems speziell des Gewerbeekzems, Arch f Dermat u Syph **173**:155, 1935, Das Maurereckzem (Eine experimentelle und klinische Studie zur Ekzemfrage), *ibid* **178**:1, 1938.

SUMMARY—It would appear that the best soap for cleansing the skin is a toilet cake soap. Basic factors constituting the eczematogenous action of soap are its defatting action inherent to excessive use and/or prolonged exposure, and prolonged exposure to alkaline salts not incorporated in soap but loosely combined as in soap powder. It is not unreasonable that the chief difference in the irritating action of toilet soap and laundry soap (in cake or bar form) is the fact that exposure to laundry soap is much more prolonged. Excluding all soap in powder form that contains alkaline salts, the role of soap used for toilet purposes as an eczematogenous substance has doubtless been exaggerated, in view of its universal and frequent use, the dilute solution of soap and its ingredients.

DETERGENTS OTHER THAN SOAP

Triethanolamine Soap—Triethanolamine forms a salt with fatty acids and may be employed to make nonalkaline base soap⁶⁰. Such soap has been suggested as a detergent to replace ordinary soap. Fiero⁶¹ studied the detergency of pure salts of triethanolamine. The following had detergent action, not as great, however, as that of ordinary soap laurate, oleate, myristate, palmitate and salts of commercial mixed fatty acids (of tallow, coconut oil and red oil). Triethanolamine salts have an alkaline reaction in aqueous solution, and therefore their use as a detergent does not overcome this objection to ordinary soap. Exceptions, however, are the salts of isocaproic, caproic, caprylic and capric acids, the p_H of which Fiero observed ranged from 6.1 to 6.4.

Acid Soap—So-called "acid" soap⁶² is made with naphthenic acids, which are recovered in the Russian oil industry from the "soda tail" obtained in the refining of petroleum fractions. Chief objections to this compound are the unpleasant smell of petroleum inherent to naphthenic acids, its low degree of hydrolysis and its poor detergent properties.

Laptev and Moldavskii⁶³ studied the action on the skin of "substitute" soaps prepared from naphthenic acids, resin acids, liquid synthetic acids, a mixture of fats with resin, and synthetic acids. It was noted that the detergent action of these preparations was less than that of ordinary soap, otherwise some of them compared favorably with ordinary soap, whereas others caused dryness of the skin or stickiness of the hair. Soaps made with naphthenic acids imparted a persistent unpleasant odor to the hair.

60 Hetzer, J. Alkalifrei Waschmittel, Ole, Fette, Wachse **9** 9, 1937.

61 Fiero, G. W. Salts of Triethanolamine, J. Am. Pharm. A **27** 658, 1938, Salts of Triethanolamine. II. Detergency, *ibid.* **28** 284, 1939.

62 Levinson, H., and Meunch, H. Naphthene Acid Soaps, Soap **14** 69, 1938.

63 Laptev, A., and Moldavskii, V. The Action of Soaps on White (Cotton) Fabric and Human Skin, Masloborino zhir delo **13** 30, 1937.

Sulfonated Oils—More recently sulfonated oils have been employed as detergents for the human skin Blank,⁶⁴ who has done pioneer work in this field, suggested this formula as a soap substitute. sulfonated mixed olive and tea-seed oil 25 per cent, light liquid petrolatum 25 per cent and water 50 per cent^{64a} The p_H of this mixture varies from 6 to 7

We studied the detergent action of sulfonated olive oil, sulfonated castor oil and sulfonated neat's foot oil mixed with liquid petrolatum We believe that sulfonated oils mixed with liquid petrolatum should be used with only a minimum amount of water We selected three formulas.

| <i>Formula 10</i> | Per Cent |
|---------------------------------------|----------|
| Sulfonated olive oil ⁶⁵ | 55 |
| Light liquid petrolatum | 45 |
| Gelatin, 25 per cent aqueous solution | 10 |

The percentage of sulfonated olive oil required to obtain a clear mixture with liquid petrolatum varies with different lots The range is 50 to 60 per cent of sulfonated olive oil and 40 to 50 per cent of liquid petrolatum For this and for the following formulas, heat the oil mixtures on a water bath until clear, then add gelatin and stir until solution is effected

| <i>Formula 11</i> | Per Cent |
|---|----------|
| Sulfonated olive oil (55 per cent) } (Formula 10) | |
| Light liquid petrolatum (45 per cent) } of this mixture | 70 |
| Sulfonated neat's foot oil ⁶⁶ | 20 |
| Gelatin, 25 per cent aqueous solution | 10 |

| <i>Formula 12</i> | Per Cent |
|---------------------------------------|----------|
| Sulfonated neat's foot oil | 45 |
| Light liquid petrolatum | 45 |
| Gelatin, 25 per cent aqueous solution | 10 |

| <i>Formula 13</i> | Per Cent |
|---|----------|
| Formula 12 | 2 parts |
| Sodium lauryl sulfate, 20 per cent solution | 1 part |

The p_H range of these mixtures was. no 10, 5.35, no 11, 5.3, no 12, 4.8, and no 13, 4.9 Gelatin was added to all the mixtures as a homo-

64 Blank, I H Action of Soap on Skin III Sulfonated Oils as Substitutes for Soap, Arch Dermat & Syph 39:821 (May) 1939

64a This preparation is commercially known as Nopco BDA (National Oil Products Co., Harrison, N J)

65 The sulfonated olive oil employed in this and the other formulas is known commercially as 75 per cent

66 The sulfonated neat's foot oil employed in this formula and in the others was acidolene A (Martin Dennis, Newark, N J.) and also the preparation of the Kali Manufacturing Co., 1410 North Front Street, Philadelphia It is clear at room temperature, becomes turbid between 50 and 60 F and solidifies between 45 and 50 F. Turbidity may be prevented by the addition of castor oil or of solvents which prevent the solidification of the fatty acids

genizing agent It enhanced the preparations from a pharmaceutical standpoint We prefer formula 12, since it is a satisfactory detergent and exerts more of an emollient action We use and recommend this formula As already discussed, we selected it to add to corn meal as a substitute for abrasive mechanic soap The odor inherent to neat's foot oil is considerably less in the sulfonated oil, so that this feature has not been an objection in our experience Formula 13, containing sodium lauryl sulfate, lathers somewhat and is perhaps a better detergent, its disadvantage being that it exerts a slight drying action on the skin

Sulfonated Esters, Ethers and Alcohols—There is increasing scientific interest in organic compounds which have wetting, penetrating, emulsifying or detergent properties These compounds, which may be classified broadly as sulfonated esters, sulfonated ethers and sulfonated alcohols,⁶⁷ have extensive use in industry There are few data available as to their use as detergents for human skin For this purpose we studied sodium lauryl sulfate and santomerse S (Monsanto Chemical Co) and a 30 per cent aqueous solution of substituted aromatic sulfonic acids The addition of one or the other of these compounds to the sulfonated oil mixtures we do not believe essentially improved them Sulfonated organic compounds exert a defatting action on the skin and are in this respect comparable to soap

The German preparation known as praecutan⁶⁸ is sold as a cutaneous detergent It consists of sodium salts of fatty acid condensation products and sulfuric acid esters of high molecular fatty acids It is a light brown liquid of oily consistency which foams with water The p_H of the preparation we determined was 5 Bauer^{68b} stated that only an insignificant number of his patients had an intolerance to the preparation

Vegetable Meals—The detergent property of oat meal flour is perhaps not sufficiently appreciated Other somewhat similar detergents, with the action doubtless attributed to the fixed oils they contain, are almond meal (sweet almond) and powdered bitter almond,⁶⁹ pow-

67 Caryl, C R, and Ericks, W P Esters of Sodium Sulfosuccinic Acid, *Indust & Engin Chem* **31** 44, 1939 von Antwarpen, F J Detergent Properties of Ether Sulfonates, *ibid* **31** 64, 1939 Tyler, C A Sulfated Fatty Alcohols, *Soap* **10** 25 (March), 21 (April) 1934 Mullen, C E The Newer Detergents, *ibid* **13** 30, 1937

68 (a) Theissen Zur Verhütung von Olekzema, *Anz Maschinewes* **59** 2, 1937 Hilgenfeldt Beitrag zur Frage der Handereinigung, *Zentralbl f Gewerbehyg* **15** 36, 1938 (b) Bauer, H Ueber Erfahrungen mit Praecutan als Wasch und Badesusatz bei Hautkranken und Hautgesunden, *Med Klin* **2** 1176, 1937

69 Bitter almond is toxic if ingested

dered soap tree bark (quillaja), powdered orris root⁷⁰ and to a lesser degree flaxseed meal. When these substances are used with water to cleanse the hands the result is relatively satisfactory. The detergent action of powdered orris root, we believe, is not generally known. Oat meal flour, especially when used with boric acid solution instead of water, is a good means of cleansing the hands of patients with eczema.

Mineral Detergents—The detergent action of soap is mainly a colloidal phenomenon conditioned by its physical properties, especially its power of lowering the surface tension and emulsifying oils. Other substances having the same physical properties of soap exert detergent action. Some minerals belong in this category and are employed as detergents alone or incorporated in soap: colloidal clay, fullers' earth (mixtures chemically allied to clay), soapstone (French chalk, "Kheel"), sodium silicoaluminates (containing aluminum, silicon dioxide [silica] and alkaline earths), silicates of sodium, sodium carbonate, sodium bicarbonate, sodium sesquicarbonate, sodium borate (borax) and disodium and trisodium phosphates. The employment of some of them in soap has been patented.

ILLUSTRATIVE CASES

ABUSE OF SOAP

CASE 1—An employee in the laundry of a hospital, in order to avoid contracting some disease (?), washed his hands each time he handled soiled dry linen. He estimated he washed his hands twenty-five to thirty times a day with the soap used in the laundry. He informed us that he could work with canvas gloves and could wear protective sleeves.

CASE 2—An employee in a dye house informed us that he, as well as the other employees, washed their hands with the soft soap used in their shop to scour wool.

CASE 3—A woman employed in making desk pads experienced a dermatitis of both hands. She glued leather on linoleum. On account of the glue adhering to her hands, she immersed them in a basin containing soap and water about a hundred times daily. She has been doing the same work for three years.

TURPENTINE AND KEROSENE TO CLEANSE HANDS

CASE 4—A woman in a printing shop used turpentine and kerosene for many years in order to remove stains from her hands and forearms. We treated her for dermatitis involving these areas. A patch test with turpentine gave a positive reaction.

PAINT SOLVENT TO CLEANSE HANDS

CASE 5—A workman spraying lacquer on furniture with a squirt gun presented dermatitis on the hands and forearms. To remove lacquer from his hands and forearms he has employed paint solvent for four years.

70 Orris root is an allergenic substance.

SCOURING POWDER TO CLEANSE HANDS

CASE 6—An employee in a hat factory presented dermatitis on both hands. He handled dyed hats which stained his hands. For three years he had removed such stains by using a scouring powder. All his fellow-workers used this powder, which they obtained from the janitor, who used it to clean lavatories.

CASE 7—A man employed in a carpet factory to clean looms presented acute dermatitis on the hands and arms. In order to remove grease, he washed with a scouring powder which was used to scrub floors. The dermatitis appeared after the initial use of this powder.

CALCIUM HYPOCHLORITE TO REMOVE DYE

CASE 8—An employee in a dye house presented dermatitis on the hands and forearms. For twenty-five years he had been handling dyes. He washed his hands about twenty times a day, using an abrasive soap and also the soap used to wash yarn. To remove stains from his hands about three times weekly he used a solution of calcium hypochlorite (hypochlorite of lime) employed in his work.

ONE USE OF GLOVES

CASE 9—In a tannery girls were employed applying "seasoning" by hand. Some used a brush, others, a rag. Gloves were worn only when the seasoning contained dye and then only to prevent the finger nails from being stained. The wearing of gloves was satisfactory. "Seasoning" used on finished skins contains water, mineral pigment, blood albumin, casein, castor oil, formaldehyde as a preservative and at times dyestuff.

IMPROVISED PROTECTIVE SLEEVES

CASE 10—An employee in a tannery told us that he and his fellow-workers on their own initiative used discarded inner tubes of automobile tires as protective sleeves.

PINE TAR AND AXLE GREASE

CASE 11—In a tannery the men known as "beamers" applied pine tar and axle grease to their hands before working. The work involved trimming wet delimed pelts with a knife on a wooden beam. The skin of the fingers of these men was white, puckered and considerably macerated. The reason given for the use of pine tar was as a protection against lime. It had been thus employed in that shop, according to the oldest employee, for fifty years. Axle grease was used to waterproof the skin. The use of pine tar to dry the fingers, permitting a better grasp of the knife handle, appeared to us to be a better explanation.

A SIMPLE PROTECTIVE MEASURE AND PRACTICE

CASE 12—The men spraying paint in a large manufacturing plant applied freely to the skin of the exposed parts, before working, cold cream supplied by the company. Goggles and respirators were also used. At the end of the work period paint literally covered the exposed skin and was easily removed by means of a clean cloth, also supplied by the company. The men stopped work ten minutes before the usual time in order to cleanse their skin.

RECOMMENDATIONS FOR A PROTECTIVE APPLICATION

CASE 13—Employees in a candy factory experienced dermatitis of the arms, which was alleged to be an expression of an allergic reaction to flour. The men

involved handled large slabs of sticky candy which they inserted into a machine that cut and packaged it. Flour was sprinkled on the slab by hand. Considerable flour dust was created when the machines were cleaned. The appearance of the eruption (with follicular involvement) suggested a dust-borne irritant flour as the cause. Pending installation of a ventilator, the application of formula 7 on the arms before working was one of the recommendations we made. Protective applications had to be dry and nongreasy. The formula has now been used for seven months. The incidence of dermatitis following its use has been decreased.

RECOMMENDATIONS FOR A PROTECTIVE APPLICATION

CASE 14—Dermatitis of the hands and forearms appeared among employees engaged in nickel-plating electric utensils. The men immersed a frame holding the utensils in a tank containing a steaming solution of a proprietary compound. The exact composition of this compound was not known, but it was thought to contain sodium hydroxide, trisodium phosphate, sodium carbonate and sulfonated alcohol. The men worked with their sleeves rolled up and with their hands and arms exposed to the steam and mist from the solution. Dermatitis appeared after variable periods of exposure. Some employees, however, regardless of prolonged contact never had dermatitis. We determined by patch tests of normal persons (not employees) that the factor in question was a primary cutaneous irritant. It was not practical for the men to wear gloves, and we were informed that it was not possible (?) to ventilate the tank containing the solution. It was recommended that (1) consideration be given to employing Negroes, (2) protective sleeves be worn,⁷¹ (3) candidates for employment who gave a history of ever having eczema or who were blondes would not be appropriate for this work, (4) such men be employed who gave negative reactions to patch tests with the control substances used in patch tests and (5) protective applications to the skin be employed. Formulas 7 and 9 were suggested. Selection of the one to be used was to be made after a trial of each formula.

SUMMARY

The role of cleansing agents applied to the skin in causation of industrial dermatitis is discussed.

The results of studies of methods employed by workmen to cleanse their hands are presented. These studies emphasize the importance of mechanical devices in the prevention of industrial dermatitis and the need of education of workmen and others concerned in preventive measures, especially in the care of the skin and in harmless methods of cleansing it.

Protective medicinal applications to the skin (protective hand creams) in prevention of industrial dermatitis are discussed. Eight formulas of protective medicinal applications, comprising greasy and nongreasy preparations and those that dry leaving a film are given.

Other protective applications (applied before working) are discussed. These essentially utilize (a) hydrous wool fat for protecting

⁷¹ Those of the type known as leatherettes (Milburn Manufacturing Company, Detroit) were recommended.

from the carcinogenic action of mineral oils and tars, (b) different applications to prevent dermatoses from petroleum and lubricating oils, (c) bland oils to facilitate removal of paint, ink and dirt and (d) sodium bisulfite (NaHSO_3) as a neutralizing and reducing agent

Harmful and harmless methods of cleansing the skin are discussed. A 10 to 30 per cent solution of sodium hyposulfite and a 0.5 per cent solution of sodium metasilicate are stressed as harmless agents for removing such substances as paint, ink and dye and as general cleansers.

A formula consisting of a mixture of sulfonated neat's foot oil, liquid petrolatum and corn meal is given as a substitute for mechanic abrasive soap.

The action of soap on the skin is discussed, including mechanic soap and its ingredients, toilet soap, neutral soap, soaps for household and laundry purposes, soap fillers, silicates of sodium, the allergenic action of soap and soap as a primary cutaneous irritant. Soap is not sufficiently soluble, as employed for toilet or laundry purposes, to permit the alkaline salts it contains, especially sodium carbonate, in sufficient concentration in soap solution to act as cutaneous irritants. Exceptions are soaps in powder form mixed with sodium carbonate.

Detergents other than soap are discussed: triethanolamine soap, naphthenic acid soap and sulfonated oils. Formulas of different combinations of sulfonated olive oil, sulfonated neat's foot oil, gelatin and liquid petrolatum and one containing sodium lauryl sulfate are proposed as soap substitutes. Sulfonated esters, sulfonated ethers and sulfonated alcohols as cutaneous detergents are discussed, as are certain vegetable meals and a variety of minerals.

1934 Spruce Street

1934 Spruce Street

1801 Pine Street

ABSTRACT OF DISCUSSION

DR EARL D. OSBORNE, Buffalo. Dr. Klauder and his collaborators have presented a great deal of material of practical value to dermatologists handling cases of industrial dermatitis. I am sorry they did not have time to say more about sulfonated oils, sulfonated alcohols and aryl alcohols now appearing on the market.

The first problem in the prevention of industrial dermatitis is the prevention of contacts with irritants and sensitizing substances handled in industry. I agree that in the majority of cases industrial dermatitis is due to the use of various cleansing agents rather than to specific substances used in industry. It is therefore essential that dermatologists should prescribe and compound suitable preparations that workmen can apply to prevent contact with irritants and sensitizing substances. They should also advise the use of nonirritating cleansing agents, such as Dr. Klauder and his co-workers have enumerated, rather than the strong alkaline and abrasive substances now in use. In addition to various substances

which these authors have already mentioned, there is one other simple preparation of great value in the prevention of industrial dermatitis and that is paraffin ointment B P, which consists of 3 per cent yellow wax (beeswax) and 20 per cent hard paraffin in petrolatum. This is a white, relatively nongreasy preparation and should be applied three or four times during the working day. In those industries requiring the application of an impervious material to prevent contact with certain substances, a base consisting of 20 per cent glyceryl monostearate, 5 per cent glycerin and 5 per cent spermaceti in distilled water and incorporating from 10 to 20 per cent of zinc oxide or some other impervious material offers an excellent nongreasy protective preparation.

In the line of cleansing agents, the new sulfonated oil recommended by Dr Blank⁶⁴ is a good preparation. The suggestion of Dr Klauder and his co-workers regarding the incorporation of cornmeal is excellent. At the present time my associates and I are in the midst of testing with sulfonated oil and sulfonated alcohol a large group of persons with normal skins and another series of persons who have various types of dermatitis. To date, we have tested approximately 100 persons with normal skins with the sulfonated oil mixture just mentioned, with negative results. Of a group of 100 persons who had a preexisting or coexisting dermatitis, there were 2 with positive reactions. So far we have seen no exaggeration of an industrial dermatitis from the use of sulfonated oil as a cleansing agent. Recently, we have been experimenting with sulfonated lauric alcohol, which can be easily made into cake form and is therefore much more practical than a liquid oil preparation. We have tested 30 persons having some sort of a dermatitis with this preparation, with two strongly positive reactions. Sodium aryl sulfate is another new substance which has been used commercially in the textile industry for its detergent quality and is similar to sulfonated lauric alcohol. To date, we have had one severe reaction from this substance. It is therefore evident from our experience that so far the sulfonated oils in Dr Blank's mixture (olive and tea-seed oils) are satisfactory, with only a slight chance of the production of a dermatitis in persons who have had a preexisting dermatitis, whereas the use of sulfonated lauric alcohol and sodium aryl sulfate by such persons may be attended with considerable danger of the production of a severe dermatitis.

DR C GUY LANE, Boston. I was much interested in Dr Klauder and his co-workers' classification of these cleansing agents which have a degreasing effect and also in their classification of the preparations they have been working on. These classifications will be of great help not only in industrial work but in other types of dermatologic work. I subscribe wholeheartedly to all that they said with regard to safety engineers. Such engineers have a far better conception of preventive measures dealing not only with general industrial hazards but with dermatologic conditions in industry than the average industrial physician or surgeon working in large or small plants part or full time. I was glad to hear Dr Klauder and his associates emphasize the necessity of education in this subject, not only education in the care to be employed in the selection of materials to be used and in the method of using them but education of workers in the use of these materials as prescribed by the safety engineer or by the particular firm. I have been interested in watching the work of Dr Blank on this subject. Dr Klauder and his associates have already reviewed the two phases of his work: first, with reference to fatty acids and varying pH concentrations on the skin and, second, with reference to the use of sulfonated oil compounds as detergents. These can be used by persons who are sensitive to soaps which contain alkali. Work is now

under way to develop a preparation for the use of certain surgeons who have a sensitivity to soap. One criticism of sulfonated oil has been that it has a drying effect. I was much interested in the fact that Dr. Klauder and his associates recommend elimination of the water entirely in sulfonated oil preparations and prefer using a high percentage of oil and the addition of corn meal, which should be an improvement.

DR. HIRAM E. MILLER, San Francisco. I should like to ask Dr. Klauder whether he has used protective creams in routine dermatologic practice. The protection of preexisting lesions of the skin is of value in some instances.

DR. JOSEPH V. KLAUDER, Philadelphia. I do not believe that the dermatologic investigation of detergents has followed the progress made in industrial detergents. There is need for chemical investigation to provide better methods of cleansing the soiled hands of workmen. I doubt if any chemist has given thought to this. My co-workers and I discussed a number of detergents, especially silicates of sodium. Sodium silicate is an important detergent used in industry. I do not believe that there has as yet been sufficient investigation of the sulfonated esters, ethers and alcohols as cutaneous detergents. The German preparation "praecutan" belongs in this group and is to my knowledge the only one that is commercially available. I hope our paper will serve as a plea for greater attention to the matter of cutaneous detergents and for investigation of methods to remove grease, stain and other material from the skin. In answer to Dr. Miller, we have sometimes used protective applications when treating patients with eczema, and I think that such applications have been effective.

PEMPHIGUS

EXPERIMENTAL STUDIES ON THIRTY-FOUR PATIENTS

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This communication is a summary of certain data obtained from the study of 34 patients with pemphigus. All the patients were admitted to the outpatient department or to the wards of the Massachusetts General Hospital between 1935 and 1939, inclusive. The ages varied from 4 to 76. There were 19 men and 15 women. The nomenclature of the types of pemphigus which we have used and will retain in this discussion varies somewhat from that in contemporary textbooks. The pemphigus in our patients has been classified simply as acute or chronic.

The acute form may be distinguished clinically by the early development of lesions in the mouth, a rapid, fulminating course, racial susceptibility (8 of the 10 patients with acute pemphigus in our series were Jews) and a high incidence in the fourth and fifth decades of life. Further, this form may be distinguished chemically by certain abnormalities in the acid-base balance of the blood. Chronic pemphigus, on the other hand, progresses slowly and may have prolonged asymptomatic periods. If lesions develop in the mouth they do so late in the course of the disease. There appears to be no characteristic racial distribution. The patients tend to be older than those with acute pemphigus. Death occurs from a disease other than pemphigus. The chemical constituents of the blood generally are within the average range for normal persons. In the group to be discussed acute pemphigus was diagnosed in 10 patients and chronic pemphigus in 24 patients.

It seems particularly desirable to emphasize that the patients with acute pemphigus were not suffering from the disease known as malignant

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The following persons assisted in this study: Dr. C. G. Lane, Dr. J. H. Swartz, Dr. W. Lever, Dr. J. Lerman, Mr. William V. Consolazio, Mr. L. J. Pecora and Miss E. Thorogood.

or acute butcher's pemphigus. During the period of this study it is believed that we did not see any patients with butcher's pemphigus, nor was the diagnosis considered seriously in any case.

The cause of pemphigus is unknown, although various investigators have attempted to implicate bacteria and viruses. A critical appraisal of several studies finds the question still unanswered. Concerning the pathogenesis, however, there is some agreement, and acceptable evidence indicates that pemphigus is intimately associated with one or more metabolic disturbances. As early as 1906 Cassaet and Micheleau¹ suggested a dysfunction of water and salt metabolism in patients with this dyscrasia. Baumm,² Stumpke,³ Urbach,⁴ Kartamischew⁵ and others have confirmed the observations. Many of the conclusions, however, were based on assumptions and were not derived from experiments. Recent improvements in the methods for determination of concentrations of acid-base constituents in biologic material and volume of body fluids have enabled us to complement previous observations.

The division of our observations into several categories is arbitrary but convenient for presentation. The abnormalities in the concentrations of the constituents of the blood are greater in patients with acute pemphigus than in those with chronic pemphigus. They will be discussed separately. The changes in body fluid volumes are similar for the two forms of pemphigus. They will be discussed together. A short presentation of the postmortem observations on 6 patients will follow. Specific therapeutic procedures were employed for 5 patients with acute pemphigus. An inducement of remissions is believed to have been achieved. Deductions concerning causation will conclude the presentation.

The concentrations of electrolyte and nonelectrolyte constituents in the arterial serum of a normal person are: sodium, 140 milliequivalents per liter, potassium, 4.5 milliequivalents per liter, calcium, 5 milliequivalents per liter, magnesium, 1.5 milliequivalents per liter, chloride, 104 milliequivalents per liter, bicarbonate, 25 milliequivalents per liter, protein, 7 Gm per hundred cubic centimeters, phosphate, 4 mg per hundred cubic centimeters, and nonprotein nitrogen, 30 mg per hundred cubic centimeters. The sum of sodium, potassium, calcium and mag-

1 Cassaet, E, and Micheleau, E. Sur deux cas de pemphigus traites par la déchloruvration, *Arch gén de méd* **1** 129, 1906.

2 Baumm, G. Ein Beitrag zum Kochsalzstoffwechsel bei Pemphigus, *Arch f Dermat u Syph* **100** 105, 1910.

3 Stumpke, G. Liegen beim Pemphigus Storungen der Kochsalzausscheidung vor? *Arch f Dermat u Syph* **108** 467, 1911.

4 Urbach, E. Zur Pathochemie des Pemphigus, *Arch f Dermat u Syph* **150** 52, 1926.

5 Kartamischew, A. Ueber die Oedembereitschaft bei Pemphigus vegetans, *Arch f Dermat u Syph* **143** 184, 1923.

nesium constitutes what is known as total fixed base. There is no comparable expression in current use for the sum of the acids. The sum of the acids must approximately equal the sum of the bases, however, as serum is essentially neutral in reaction. Of the constituents just enumerated, we are especially interested in this study in sodium, potassium, calcium, total fixed base, protein and nonprotein nitrogen.

The methods for the analysis of the constituents of the blood have been described.⁶ Blood and plasma volumes were determined with the photocolormeter by the method of Gibson and Evans.⁷ Interstitial fluid volumes were determined by the method of Crandall and Anderson.⁸

The concentration of serum sodium in all the patients with acute pemphigus was less than 132 milliequivalents per liter in one or more samples of serum (charts 1 and 2) which were studied during the period when oral lesions were present. Three patients with acute pemphigus shortly before death had a serum sodium concentration of approximately 120 milliequivalents per liter. These values are indicative of a profound disturbance of salt metabolism, such as may be observed in advanced chronic nephritis, diabetic coma, adrenal insufficiency or severe heat cramps. The deviation from the normal of this constituent in patients with pemphigus was associated with the severity of the clinical condition and with the mass of skin involved. Similarly, a return toward normal of the concentration of serum sodium was associated with clinical improvement and regression of cutaneous lesions. Exceptions were noted shortly before death in 2 patients who had been under observation for several months. Each had experienced at least one clinical remission with restoration of a normal concentration of serum sodium. Late in the course of the illness the serum concentrations were normal, although the clinical state was ominous.

The concentrations of total fixed base and potassium were not determined prior to 1937. Three patients with acute pemphigus studied since that time have had at most determinations a concomitant lowering of total fixed base and sodium. Exceptions were noted when changes in serum sodium were accompanied by an increase in serum potassium. The highest concentration observed in serum potassium was 12.7 milliequivalents per liter. After active treatment this value decreased to 4.9 milliequivalents per liter one week later. A subsequent return to

6 Talbott, J. H. The Interpretation of Clinical Chemical Procedures, Ohio State M. J. **35** 137, 1939.

7 Gibson, J. G., Jr., and Evans, W. A., Jr. Clinical Studies of Blood Volume. Clinical Application of Method Employing Azo Dye "Evans Blue" and Spectrophotometer, J. Clin. Investigation **16**:301, 1937.

8 Crandall, L. A., Jr., and Anderson, M. X. Estimation of the State of Hydration of the Body by the Amount of Water Available for the Solution of Sodium Thiocyanate, Am. J. Digest. Dis. & Nutrition **1** 126, 1934.

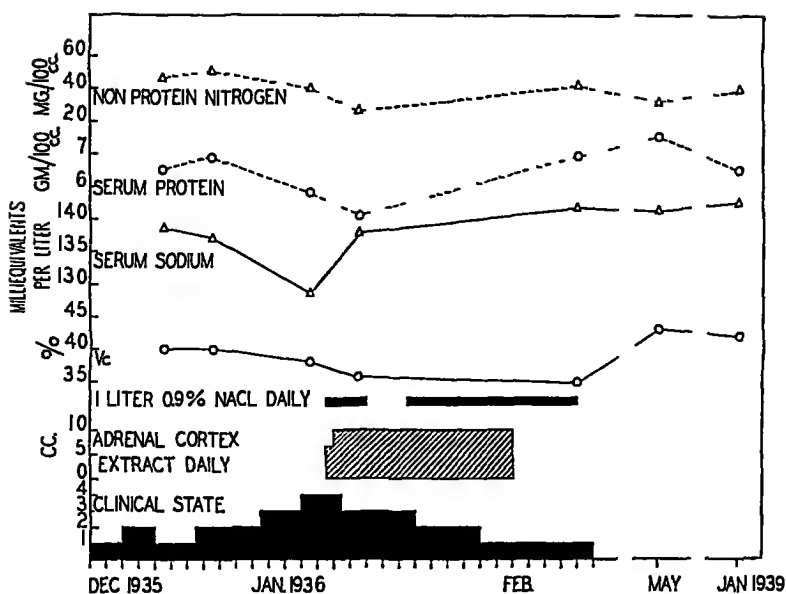


Chart 1—Experimental observations and treatment of a patient with acute pemphigus who experienced an induced remission which has persisted for more than three years

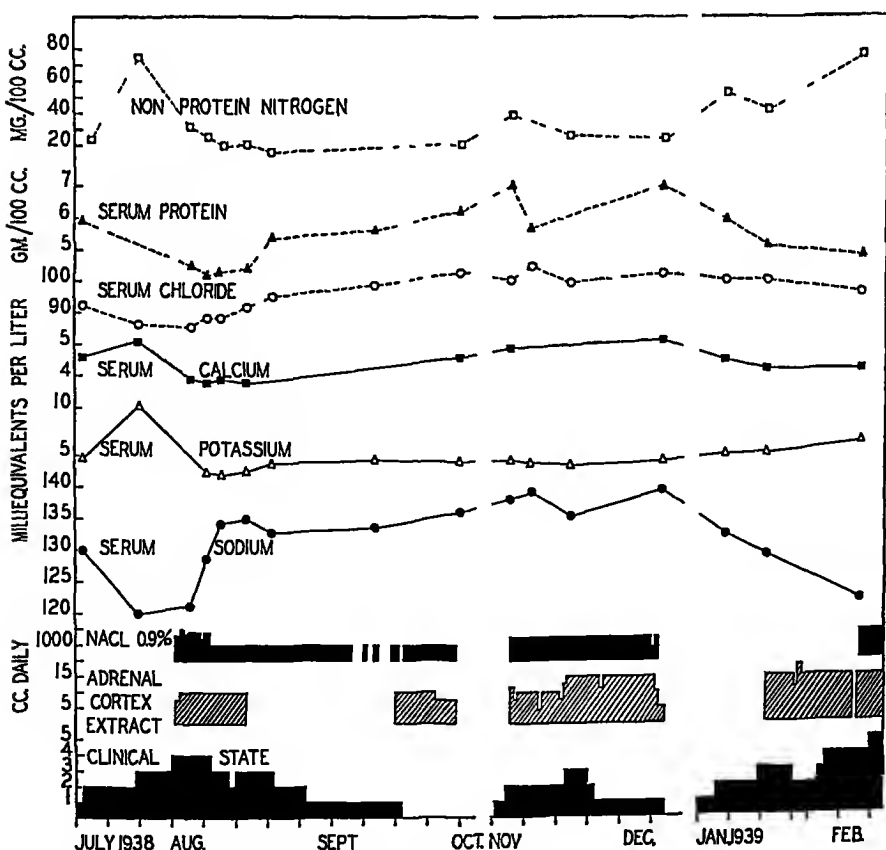


Chart 2—Experimental observations and treatment of a patient with acute pemphigus who experienced two induced remissions and subsequently died (A scale of 0 to 5 is used to represent the clinical state, 0 implies no local or general symptoms. Death occurred early in February 1939)

11.9 milliequivalents per liter was accompanied by exacerbation of cutaneous lesions

The concentration of serum calcium was diminished during a relapse in all the patients with active pemphigus in whom it was investigated. There did not appear to be a constant correlation between the level of this constituent and the clinical condition. In 3 patients it was less than 4 milliequivalents per liter for two or more weeks. In each a return toward normal followed whole blood transfusions and was not related chronologically to clinical improvement. An abnormal concentration of calcium was accompanied invariably by a diminution in concentration of serum protein. It is assumed, therefore, that the principal reduction was in the calcium bound to protein and that the concentration of ionized calcium was not appreciably altered.

The serum protein concentration was less than 5.2 Gm. per hundred cubic centimeters at least once in each patient studied. Restoration followed transfusions of whole blood when these were given. A progressive decrease with each successive relapse was characteristic. In 2 patients improvement in the clinical state was followed by restoration of protein concentration without transfusions. The concentration of serum albumin and globulin and the albumin-globulin ratio were determined in several samples of serum. A decrease in concentration of albumin with an increase in concentration of serum globulin was observed. The resulting ratios (0.6 to 1.4) were in the range noted in patients with lipoid nephrosis and edema.

The concentration of nonprotein nitrogen in the serum was normal in 2 patients and elevated in 5. The highest value observed was 75 mg per hundred cubic centimeters. During periods of clinical improvement a return toward normal was noted.

Patients with chronic pemphigus showed abnormal concentrations of constituents in the blood less frequently, the variations from normal were quantitatively smaller. Only 6 of the 24 patients in this group had a serum sodium concentration below 135 milliequivalents per liter, the lowest observed was 131. This minimal value for patients with chronic pemphigus is similar to the maximal value for patients with acute pemphigus. Determinations of the constituents of the serum were not made frequently, but the available data suggested that the mass of skin involved was not related directly to the changes in the concentration of serum sodium. Likewise there appeared to be no correlation between the level of serum sodium and the course of chronic pemphigus.

The concentration of potassium was determined in the serum of 10 patients with chronic pemphigus. The amount was above normal in only 1 sample of serum (8.2 milliequivalents per liter). The concentration of calcium was 4.5 milliequivalents per liter or less in the serum of 8 of the 9 patients for whom determinations were made; the lowest value

observed was 4 milliequivalents. The serum protein concentration was determined for 17 patients and in 7 specimens was found to be less than 5.5 Gm per hundred cubic centimeters. It was observed in cases of acute pemphigus that a diminution in concentration of serum protein was accompanied by a diminution in concentration of serum calcium. The concentration of nonprotein nitrogen was above 40 mg per hundred cubic centimeters in the serum of 4 patients, all of whom were older than 65. It is reasonable to attribute the changes to age rather than to associate them with the pathogenesis of the cutaneous lesions.

For control observations determinations were made of the acid-base balance of the blood of 9 patients with generalized eruptions other than

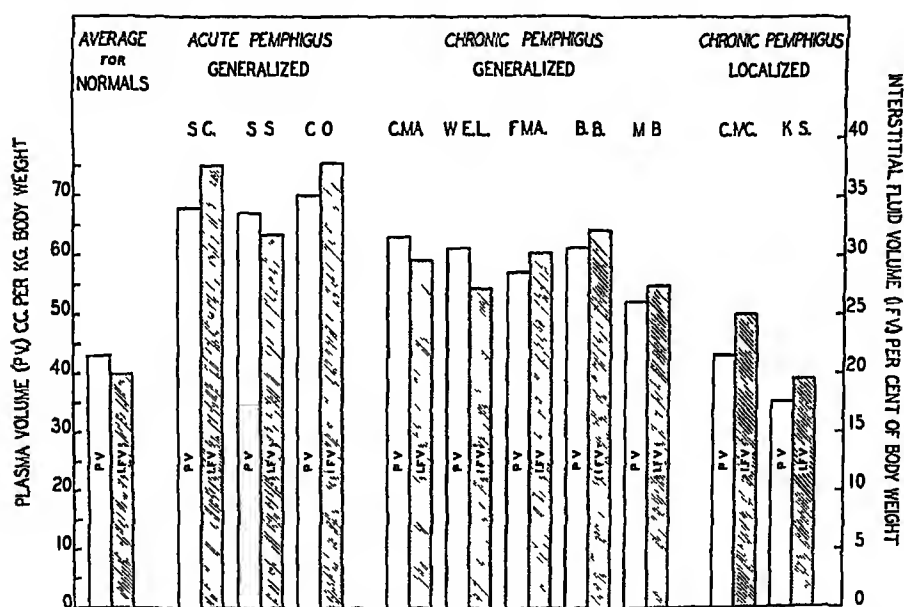


Chart 3—Observations of plasma and interstitial fluid volumes of patients with either acute or chronic pemphigus

pemphigus. The abnormal concentrations in this miscellaneous group of patients were not considered significant. It is believed, therefore, that the changes in concentration of sodium, potassium, total fixed base, calcium, protein and nonprotein nitrogen observed in the blood of patients with acute pemphigus are noteworthy.

Plasma volume, blood volume and interstitial fluid volume (chart 3) were determined for 3 patients with acute pemphigus and for 8 patients with chronic pemphigus. All patients with generalized cutaneous lesions had an increase above normal in the determined values. During the critical stage of acute pemphigus the plasma volume determinations showed increases as great as 60 per cent above the average for normal persons. Absolute changes in interstitial fluid volume were greater, although the percentile increase was less. Patients with acute pemphigus

had a 7 to 10 Kg excess of fluid in the interstitial spaces After recovery from acute pemphigus 1 patient had normal values for these constituents There appeared to be no correlation between formation of bullae and increase in volume of body fluid

Routine studies of the urine showed no evidence of renal dysfunction, such as might account for chemical changes in the blood and increase of interstitial fluid The excretion of phenolsulfonphthalein was studied in 4 cases of acute pemphigus and in 6 cases of chronic pemphigus. A normal response was noted in most instances Inulin and creatinine clearances were determined for a patient with acute pemphigus Normal data were obtained It is concluded that the metabolic changes in pemphigus may develop without glomerular or tubular dysfunction

Necropsies on 3 patients with chronic pemphigus showed no recognized changes which contributed to our understanding of the pathogenesis of the disease A serious complicating condition was noted in each instance Necropsies on 3 patients with acute pemphigus, however, revealed changes which were believed to be significant Two of the 3 patients had anatomic changes in the adrenal glands which were visible grossly and microscopically One patient had infarction of one adrenal gland and hypertrophy of both Both adrenal glands were hemorrhagic in the second patient The other endocrine glands were normal in both groups of patients

Our particular interest in treatment was confined to oral and parenteral therapy for patients with acute pemphigus The acid-base changes in the blood were consistent with adrenal insufficiency The anatomic changes in the adrenal glands of 2 patients who died with acute pemphigus appeared to confirm the pathogenesis of the chemical changes Treatment was instituted, therefore, to correct the dysfunction This consisted of administration of large amounts of adrenal cortex extract and sodium chloride solution parenterally Each of the 5 patients treated with these substances had a restoration of the concentrations of sodium, potassium, total fixed base and nonprotein nitrogen Clinical improvement followed the restoration Neither the clinical improvement nor the changes in the serum were as rapid, however, as those which are observed in the treatment of uncomplicated acute adrenal insufficiency In some cases more than a week elapsed before the development of new bullae had been checked This suggests that factors other than adrenal insufficiency are important in the pathogenesis of acute pemphigus

The duration of remission was variable and apparently unpredictable Two patients had a satisfactory remission during the first admission to the hospital, which has continued for three and one-half and three years respectively The other patients were less fortunate As long as active treatment was continued, clinical improvement was noted A relapse invariably followed cessation of treatment Resumption of treat-

ment after one or more relapses eventually was ineffective. The duration of life after the first onset of generalized eruption in this group of 3 varied from four to eight months.

In contrast to the inducement of remissions in the 5 patients treated, a similar number not treated died promptly. The longest interval between onset of acute exfoliation and death was two months, the shortest interval was eleven days. None of the patients in this group enjoyed a spontaneous remission, and once they had become chronically ill, the clinical course was one of uninterrupted regression.

Any contemporary theory of the cause of pemphigus is inadequate. The statement that pemphigus is a virus or bacterial disease is not supported as yet by acceptable evidence. If it is proved, however, that pemphigus is produced by a virus or a streptococcal infection, it would strengthen our argument concerning the pathogenesis and contribute toward a satisfactory explanation of the complete pathologic syndrome. It seems likely that infections reduce the amount of normally available adrenal cortex hormone. A micro-organism or an ultrafiltrable organism might produce the cutaneous lesions in acute pemphigus as well as impede the elaboration of the adrenal cortex hormone. If this interpretation is correct, the chemical and fluid changes in the body should be considered as secondary manifestations.

SUMMARY

Metabolic studies of 34 patients with pemphigus are reported. The patients were classified simply as having either acute or chronic pemphigus. Acute pemphigus is not to be confused with the syndrome known as malignant bullous pemphigus. Studies of the blood of the patients with acute pemphigus showed changes in concentration of constituents consistent with adrenal insufficiency. Patients with either type of pemphigus showed an increase in volume of plasma, blood and interstitial fluid.

Five patients with acute pemphigus were given supportive treatment only. Death followed in from eleven days to eight weeks after onset of acute symptoms. Necropsies were performed on 3 patients, 2 of whom showed anatomic changes in the adrenal glands. The other 5 patients with acute pemphigus were given large amounts of adrenal cortex extract and sodium chloride solution. A remission followed in each patient. This persisted three and one-half and three years, respectively, in 2 patients without further specific treatment. In the remaining 3 patients, the remission persisted only as long as active material was administered, and eventually this became ineffective.

It is believed that no contribution to knowledge of the causation of the disease has been made. Our understanding of the pathogenesis, however, is believed to be enhanced.

ABSTRACT OF DISCUSSION

DR RICHARD S WEISS, St Louis Dr Talbott has presented a study of pemphigus which is instructive and illuminating not only so far as the pathogenesis of the disease is concerned but also from the standpoint of treatment. In fact, his observations might lead one to believe that there is a modicum of renewed hope for the severely sick patients with acute pemphigus. Dr Talbott does not claim that he has a new cure for pemphigus, but his studies indicate that we may have an additional method of treatment which materially increases the chances for recovery or remission.

It is interesting to note that there are changes in the concentration of several of the chemical constituents of the blood serum in certain cases of pemphigus. I am not an expert in blood chemistry and so cannot discuss the paper from the standpoint of variations in the concentration of the constituents of the blood serum with any great degree of accuracy. However, it appears that in some instances there was a profound disturbance of salt metabolism and water metabolism, such as is seen in patients with advanced chronic nephritis, diabetic coma and adrenal insufficiency, and when measures were taken to supply the body with those constituents of serum that were necessary to restore that fluid to approximately normal concentration, the improvement in a number of the patients was quite evident.

Dr Talbott has demonstrated histologic changes in the adrenal glands of several of his patients at autopsy, and on this basis he has obtained remissions and improvement by treatment directed toward relief of adrenal insufficiency. If one can induce remissions in these patients with more or less acute pemphigus by the administration of physiologic solution of sodium chloride and adrenal cortex extract, it may be that the percentage of so-called cures will rise. Let it be emphasized, however, that these patients must be selected, that careful studies of blood chemistry must be made along the lines that Dr Talbott has indicated and that this treatment should be given only to patients who present the apparent syndrome of adrenal insufficiency.

Dr Talbott stated that clinical improvement eventually followed a restoration of the acid-base equilibrium in 5 patients but that neither the clinical improvement nor the restoration of the blood salts was as rapid as one observes in the acute crisis of Addison's disease. In fact, more than a week usually elapsed before the development of new bullae was checked. Therefore, he draws the conclusion that factors other than adrenal insufficiency are extremely important in the pathogenesis of foliaceous pemphigus. I think it is important to emphasize that they make no claim that acute adrenal insufficiency is the sole etiologic mechanism.

It seems to me that Dr Talbott has checked and guarded his experiments by showing that exacerbations occurred when the treatment was discontinued. He has apparently demonstrated that there was a diminution in the concentration of serum sodium in certain cases of pemphigus foliaceus and that there was a decrease in the total fixed bases (the chlorides and proteins) and an increase in the concentration of potassium and nonprotein nitrogen. A definite disturbance of volume changes in the body fluid was apparently demonstrated, therefore, improvement or remissions may be expected in a certain number of patients if treated on the basis of adrenal insufficiency. I hope that others may have the opportunity to make similar studies, so that Dr Talbott's observations may be confirmed in a very large series. At any rate, I believe that even this small series has given an accessory treatment for use in certain cases that may prove very valuable.

DR C GUY LANE, Boston There is always a question of the classification of pemphigus. In my opinion, Dr Talbott has done right in classifying these patients

as having acute pemphigus or chronic pemphigus. Whether one thinks of the disease as an acute fulminating type or as a more benign type lasting longer or perhaps divides it into types such as pemphigus vulgaris and pemphigus foliaceus, one can still observe, and perhaps more correctly, the classification which the authors have adopted for the present discussion. There is not yet any satisfactory etiologic classification, but there is beginning to be the suggestion of a classification, perhaps as a result of therapy. For example, consider further the two groups of patients with acute pemphigus, those who were untreated and died within a comparatively short time and those who, with therapy carried on in accordance with the chemical findings, had remissions coincident with treatment but eventually did not respond. Here is a possibility of grouping certain patients with the acute form of the disease by their response to therapy. Another group includes those who respond to the Davis treatment, and then there are a few patients who have also responded after treatment with dihydrotachysterol.

It has been interesting to watch the subsiding of cutaneous involvement as treatment has progressed, to see the less frequent appearance of bullae and eroded areas, a gradual improvement in the general condition of the patient, finally only scarring and pigmentation and eventually complete recovery. It has been a most striking clinical picture as the treatment has progressed.

It seems possible that this work may indicate another type or another subdivision of what is at present called pemphigus, resulting perhaps from organic manifestations similar to those discovered in the adrenal glands.

I said there is no satisfactory theory with regard to the origin of pemphigus, and perhaps it is dangerous to propose one. At the same time, let me review some of the ideas which have been mentioned in the last few years. The Pels-Macht test has given a certain amount of information and indicates perhaps an influence by a toxin in the blood. The Ashton-Welsh test also shows evidence of a toxic factor, indicated by the speed of streptococci in responding to electric current. These two suggestions indicate the possibility of streptococcic involvement. There have been a few cases reported in which improvement followed the administration of sulfanilamide, but these results have not been consistent.

It is a known fact that large bullous lesions are produced on the skin in impetigo and erysipelas. Again, perhaps this indicates a relation to the streptococci. Perhaps the correct theory of the cause of pemphigus has not been advanced, but I think Dr. Talbott has given definite aid in the diagnosis, classification and treatment of a certain type.

DR M. F. ENGMAN, St. Louis. This type of work is much needed not only in the study of pemphigus but in the study of many diseases. It is a new kind of approach to these problems.

My associates and I have been interested in certain chemical studies too. Dr. Ross MacCardle has been working at the Barnard Free Skin and Cancer Hospital with microincineration and spectrographic studies of minerals in the skin. He has been studying normal subjects of different ages and is beginning to get a picture of the normal skin at various ages. He has observed, for instance, that the amount of silicon seems to decrease with age. Curiously, in the skin of some patients with pemphigus he noticed a marked increase in silicon. These patients were elderly, and it was remarkable to find a greater amount of silicon than that normal for that time of life. This, of course, is a preliminary observation, and no conclusions may be drawn from such isolated instances.

DR M. B. SULZBERGER, New York. At the suggestion of Dr. Joseph Goodman, of Boston, I asked Dr. Talbott for the details of his treatment consisting of the

administration of adrenal cortex extract and saline solution I had a patient with what seemed to be acute pemphigus. Unfortunately there was no beneficial effect from the treatment. I was unable to study the blood chemistry or to study the tissue fluids or blood plasma. However, I followed the treatment that he had outlined as closely as I could. The patient died about nine to ten weeks after the onset of acute symptoms. If one assumes that I treated my patient the way Dr Talbott has treated his patient, and if one further assumes that my patient had the same condition as did those Dr Talbott treated with the combination of adrenal cortex and salt solution, then the result in my case must be regarded as a failure of the method. However, totaling Dr Talbott's results with mine gives 5 good results out of 6 trials, and that is still a very impressive figure in acute pemphigus. I hope that results continue in that proportion. However, I think that dermatologists must somewhat revise their ideas concerning the prognosis of pemphigus in general. One continually sees, hears and reads of new instances of isolated patients with pemphigus getting well with various forms of therapy. I think today one must say that while the prognosis of pemphigus is bad, it is not hopeless. Some patients with true pemphigus recover, and this seems to be true in younger persons and particularly in native Americans.

DR THEODORE CORNBLEET, Chicago. I observed a low store of vitamin C in patients with pemphigus. Because of this observation I gave this vitamin to these patients and found that it had supportive value. The patients apparently were buoyed up and stimulated by such treatment. Soon after the patients received sufficiently large amounts of vitamin C, the characteristic, offensive fetor emitted by persons with pemphigus was decreased or abolished. I found this fact of value in obtaining improved nursing care for them. This form of therapy does not alter the eventual course of the disease, because the patients die anyhow.

DR JOHN H TALBOTT, Boston. I appreciate Dr Sulzberger's follow-up report on the patient who was treated with adrenal cortex extract later in the disease. It appears from the investigations made by my associates and me that the patients with acute pemphigus who respond are those treated early. The 2 patients with this form of pemphigus that are now alive, more than three years after their acute illness, were seen early in the disease. The chemical studies were completed and treatment was instituted before they had become gravely ill.

The matter of classifying the various forms of pemphigus is not settled, nor will it be easy for the majority of observers to agree on any one system of classification. We believe that our classification has merit because it is based on chemical abnormalities and clinical findings. It might be of interest to mention that during the past five years we have seen at least 4 patients with generalized exfoliation who would have been considered to have an acute form of the disease if the clinical course only had been considered. Abnormal concentrations of serum electrolytes were not observed in these patients, however, and we treated them for chronic pemphigus. Their subsequent course justified this presumption.

I shall refer briefly to some negative results we have obtained with various purified vitamins. More than four years ago we employed large amounts of vitamin C orally and parenterally in 2 patients with acute pemphigus and in at least 1 with chronic pemphigus. It was concluded at that time that the effect was negligible. Recently we used thiamin chloride, nicotinic acid and riboflavin, as well as vitamin C, with apparently similar results. It is possible that we did not use sufficient amounts for a sufficient length of time, but judging from the amounts necessary for therapeutic benefit in cases of known avitaminosis, adequate quantities were given.

TREATMENT OF RINGWORM OF THE SCALP WITH GENTIAN VIOLET

W F SPILLER, M D

W B SHARP, M D

AND

M B JOHN, M A

GALVESTON, TEXAS

Treatment of tinea with a fungicidal dye was suggested some years ago by Castellani,¹ who painted carbolfuchsin in ringworms of the foot and of the groin. For lesions secondarily infected or moist, he recommended this rather than methods of treatment in common use.

Dyes do not have as powerful fungicidal as bactericidal property. Farley² found that dermatophytes tolerated greater concentrations of gentian violet than bacteria and used the dye in his mediums for the isolation of fungi, to retard bacterial contamination. Cultures of various microsporons and trichophytons on Sabouraud's agar withstood concentrations varying from 1:166,000 to 1:41,000. Of the several dyes that may be used, neither fuchsin nor gentian violet is the most strongly inhibitive to fungus growth. With concentrations similar to Farley's, Leonian³ found the restraint erratic, owing to technical variations, but definitely greater with malachite green than with gentian (crystal) violet.

McCrea's⁴ cultures of trichophytons and epidermophytons were inhibited by brilliant green but not by gentian violet or basic fuchsin.

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Read before the Section on Dermatology and Syphilology at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

1 Castellani, A. (a) Carbolic Fuchsin Paint in the Treatment of Certain Cases of Epidermophytosis, *Am Med* 23:351, 1928, (b) Further Observations on the Treatment of Epidermophytosis of Toes and Certain Other Forms of Epidermophytosis by a Fuchsin Paint, *J Trop Med* 32:77, 1929.

2 Farley, D. L. Use of Gentian-Violet as a Restrainer in the Isolation of Pathogenic Molds, *Arch Dermat & Syph* 2:459 (Oct) 1920.

3 Leonian, L. H. Effect of Position of Inoculum on Growth of Some Trichophytons in the Presence of Dyes, *Arch Dermat & Syph* 25:1016 (June) 1932.

4 McCrea, A. Fungicidal Value of Some Common Dyes Against Dermatophytic Fungi, *Mycologia* 26:449, 1934.

in equivalent concentrations. On the other hand, Schamberg and Kolmer⁵ found that while brilliant green was the best restrainer of growth, the violet dye was superior as a fungicide.

FORMULA SELECTED

Our selection of a dye for the experimental treatment of *tinea capitis* rested less on *in vitro* fungicidal potency than on toleration of the dye by the tissue and effectiveness of the dye in the tissue. We employed concentrations a thousand times greater than those exhibiting differential fungistatic effect. We first tried, without success, a formula with bismuth violet, then newly reported⁶ as effective in the treatment of wounds. Success had been widely acclaimed for gentian violet as an antiseptic for application to infected tissue, not only as a bactericide⁷ but also as a parasiticide⁸ and as a fungicide⁹. We adopted a formula consisting of 2 per cent gentian violet and 10 per cent salicylic acid in 95 per cent alcohol.

TREATMENT

The affected head was first shaved, cleared of all crusts with soap and water and then alcohol and painted with the gentian violet and salicylic acid solution. The treated area assumed a gaudy hue. This aspect of the treatment was found objectionable by Castellani in his treatment of epidermophytosis, though it was less so in our case, as the head remained covered to minimize contagion. Daily for a period of ten days the lesion was similarly scrubbed clean and painted. The medication caused crusts to form which tended to shield the lesion from further applications, and these crusts had to be removed. We attribute the better results obtained in private than in clinical patients to a more thorough preliminary cleansing, the former were treated by one of us, after preparation by a nurse, and the latter by medical students or by some one in the home.

RESULTS

Over three fourths of our patients were from the outpatient clinic of the University of Texas School of Medicine. As is expected of such a clientele, some did not cooperate well or return for the desired period

5 Schamberg, J. F., and Kolmer, J. A. Studies in the Chemotherapy of Fungus Infections, *Arch. Dermat. & Syph.* **6**:746 (Dec.) 1922.

6 Barksdale, I. S. The Use of Bismuth Violet in the Prevention of Wound Infection, *South. Med. & Surg.* **91**:597, 1929.

7 Burke, V., Jessup, M. P., and Philips, S. Choice of Antiseptic Dye in Mixed Infection, *J. Infect. Dis.* **43**:131, 1928.

8 Faust, E. C. Parasitical Potencies of the Tri- to Hepta-Methyl Derivatives of Rosanilin, *Proc. Soc. Exper. Biol. & Med.* **26**:748, 1929.

9 Gomez-Vega, P. Mycostatic Studies on Certain Moniliae and Related Fungi, *Arch. Dermat. & Syph.* **32**:49 (July) 1935.

of treatment and observation, and cannot therefore be included in our report. In our opinion their response to the treatment, so far as it went, resembled that of the patients here reported on.

The effect has proved more satisfactory than that of other topical medications which we have employed. By "fully satisfactory effect" we mean a prompt response, with evident subsidence of clinical manifestations within two weeks and continued progress to complete recovery. Absence of evident response for a month is noted as unsatisfactory.

Our totals might suggest that ringworm of the scalp shows a fairly good response regardless of mycologic type. With 65 patients suffering from tinea capitis, we found a fully satisfactory response in 37 and a fairly satisfactory response in 10. We thought at first that the treatment was proving suitable for tinea capitis in general. The completed mycologic analysis shows, however, that the infections in our patients were due predominantly to microsporons of the animal type and that those due to microsporons of the human type or to trichophyton did not respond well. Microsporons of the animal type account for a much larger proportion of the cases of ringworm of the scalp in Galveston than reports indicate for some other localities. We read that in a majority of the instances cited by Ebert¹⁰ microsporons causing the infections were of the human type, in a Montreal series¹¹ they were about equally of the animal and of the human type, and in an outbreak at Winnipeg¹² they were almost entirely of the human type. In contrast with this, in a series of 116 cases in Galveston in which the lesions yielded fungi infective to the scalp, we found *Microsporum felineum* (*Microsporum lanosum*) in 68 infections, *Microsporum audouinii* in 16 and other species of *Microsporum* or *Trichophyton* in 32.

As the response of the respective mycologic types of ringworm has differed, we present our observations for each type separately.

Tinea Due to Microsporons of the Animal Type—The most significant results were those in patients infected with microsporons of the animal type, the most common in our locality. Two thirds of the aforesaid 68 infections with *M. felineum* involved the scalp (others the face and neck and occasionally the extremities or trunk), and 30 of them, all in children, were treated with the gentian violet and salicylic acid preparation and were under observation long enough to show the result.

10 Ebert, M. H. Ringworm of the Scalp, *M. Clin. North America* **19** 1241, 1936.

11 Burgess, J. F. Fungus Infection of the Skin. A Cultural Study of the Flora of Ringworm, *Arch. Dermat. & Syph.* **12** 853 (Dec.) 1925.

12 Davidson, A. M., Gregory, P. H., and Birt, A. R. Treatment of Ringworm of the Scalp by Thallium Acetate and the Detection of Carriers by the Fluorescence Test, *Canad. M. A. J.* **30** 620, 1934.

The mycologic and clinical manifestations were in all respects typical and seemed representative of infections with the animal type anywhere. Colonies of *M. felineum* appeared within a few days on Sabouraud's insulation medium, first circular and radiating, and later developing a downy surface growth that became loosely woolly. All strains showed a yellow-orange color of the under surface and a diffusible yellow pigment. The fully developed colony, apart from pleomorphic changes, was roughly circular and several centimeters across, with a surface powdery at the center and woolly toward the periphery. Within a month pleomorphism set in, snow white mycelium appeared in downy tufts, spreading rapidly into a medallion or radial branching effect and eventually in many instances covering the entire colony.

Morphologically, there developed on lateral branches enormous numbers of large spindle-shaped macroconidia, thick walled and spiny, averaging about 75 microns in length and 15 to 20 microns in width and containing from three to twelve cells. There also were club-shaped microconidia about 5 by 2 microns. The mycelia structure was typical, with raquet segments. As cultures became pleomorphic, chlamydospores became abundant, while the macroconidia and later the microconidia decreased and finally disappeared.

The lesions were maculosquamous, irregularly circular and more often multiple than not. They usually measured from 0.5 to 2.5 cm across, with some smaller and some much larger. Hairs within their bounds turned white and broke off. There was sometimes secondary infection, crusting or other inflammatory sign.

Of the 30 patients whose lesions were treated with our gentian violet formula, the response in 21 was prompt and fully satisfactory, in 3 others it was less prompt but fairly satisfactory. The lesions of the remaining 6 did not respond well, on 2 the treatment was continued for two or three months (on 1 with much eventual improvement), while on the other 4 another treatment was substituted after two weeks, when this one seemed a failure. The patients whose lesions did not react well were slightly younger than the others, averaging about 6 years of age as compared with 7 years for all patients observed. Their lesions did not differ significantly in grade, extent of spread, secondary infection, any clinical indication of severity or in mycologic findings.

Nearly all the patients with ringworm due to microsporons of the animal type that came to us during this period have been so managed, and we cannot compare them with controls otherwise treated. Most of those not handled in this manner were epilated. Those that received other local applications did not show as favorable results, on the average, but they were too few for us to make significant comparison. Recalling

our experience before instituting the gentian violet treatment, we regard this as distinctly the most successful topical medication we have ever employed

Tinea Due to Microsporons of the Human Type—We instituted the same treatment on a number of patients infected with *M. audouinii*, but on only 5 did we continue it long enough for any extended observation. The response was unsatisfactory in all but 1, and that patient was 11 years old and nearing the usual age for spontaneous recovery. Of the 4 in whom the results were noted as unsatisfactory, after a number of weeks 2 showed a favorable response, 1 eventually had the treatment changed and 1 finally lapsed from treatment, uncured. As a rule, we changed early to other kinds of treatment, thinking it unfair to continue one that was evidently inferior.

Ringworm due to microsporons of the human type has been found refractory to other topical medications that are successful with the animal type, even when these have been continued for months. It requires instead epilation by roentgen rays or some other means.¹³ The lesions produced by the animal type tend to heal spontaneously in time, whereas those caused by the human type do not undergo spontaneous cure except with approach to puberty. With some exceptions,¹⁴ neither type affects the adult.

These few cases are admittedly inadequate to establish the presumed negative value, particularly as the human type of tinea in our locality is culturally atypical. We have seen colonies with the central button, radial grooves and other characteristics commonly described, but our more usual colony grows into a flat, even bordered circular disk, with a feltlike surface and a color ranging from white to buff, often with concentric rings of deeper shade. The resemblance is sufficient for identification as *M. audouinii*. The colony grows more slowly than that of *M. felinum*, and the pleomorphism, so common in the latter species, occurs only exceptionally. The microscopic structure is similar except that macroconidia are rarely found and are smaller than those of *M. felinum*. The lesion produced by this organism does not differ in appearance from that already described for the animal type, and only by laboratory observations can we distinguish the one from the other.

Tinea Produced by Trichophyton—The ringworms of the toe and groin, which Castellani¹⁵ reported as responsive to treatment with dye, were presumably trichophyton or epidermophyton infections. We watched the response to gentian violet treatment in a few cases of tinea

13 Wise, F., and Wolf, J. The Pharmacopeia and the Physician. The Use of Dermal Parasitocides, J. A. M. A. 107 1126 (Oct 3) 1936.

14 Fox, H., and Fowlkes, R. W. Ringworm of the Scalp in Adults, Arch. Dermat. & Syph. 11 446 (April) 1925.

capitis due to trichophytons. These infections differed in appearance from those caused by the microsporons and somewhat among themselves. They frequently presented a more granular or gutlike form of scaling and were more widely disseminated over the scalp, without as definite localization in circumscribed patches. Hairs within the affected areas were not so uniformly discolored and broken.

From the literature we had little hope of success, especially with the endothrix species. Farley² found that a trichophyton could withstand greater concentration of gentian violet than either of the two microsporons, and Lewis¹⁵ found that the endothrix is peculiarly resistant to fungicidal applications. *Trichophyton violaceum* has received more attention than the others. It caused most of the ringworm of the scalp in adults reported by Chen and Kurotchin¹⁶ in Peiping. Lewis and Hopper¹⁷ reported that the ringworm caused by trichophyton offered greater resistance to treatment than that due to either of the microsporons, even *M. audouinii*, and had greater tendency to relapse after depilatory measures. The only case in which we recovered *T. violaceum* was that of a small child with kerion, a complicated lesion for which we employed other medicinal treatment as well as the application of gentian violet. The treatment was successful.

We had a number of patients with infection of the scalp caused by a variety of *Trichophyton epilans* and treated 10 by this method. Our strains had the characteristics usually recorded for *Trichophyton cerebri-forme*. The colony began as a small puff, and as it spread convoluted folds developed, with irregular radial grooves toward the center and a border fringed with radial spines, largely submerged. Most of our potassium hydroxide mounts showed endothrix arrangement of arthrospores. Often the lesions seemed virulent, sometimes extensively disseminated and numerous and sometimes red and swollen, containing yellowish pustules. Infections elsewhere on the body had a similar inflammatory character, the localization on the scalp being rather exceptional. A prompt and satisfactory result was obtained in 4 of the 10 patients and a fair result in 2 others.

Infections by a few other trichophytons that localize occasionally in the scalp were so treated, though there were only 1 or 2 of each. The response most commonly obtained was one at first favorable but without progress to complete cure. The lesions were usually of the trichophyton

15 Lewis, G. M. Curability, Without Depilatory Measures, of Infections Caused by Animal Microsporons, *Am J M Sc* 189:364, 1935.

16 Chen, F. K., and Kurotchin, T. J. Tinea of Scalp Among Adults in Peiping, *Nat M J China* 17:185, 1931.

17 Lewis, G. M., and Hopper, M. E. Ringworm of the Scalp. Clinical and Experimental Studies in Types of Infection Resistant to Treatment, *Arch Dermat & Syph* 35:460 (March) 1937.

type, sometimes resembling localized and crusted seborrhoea sicca. Most of them seemed to react well until nearly cured, then they would show patches of renewed activity spreading within the affected area. In most instances the treatment was given up after this initial failure, but in 1 a more extended course was tried with eventual success.

While the gentian violet treatment in this limited number of patients with ringworm caused by trichophytons was not as a rule successful, we are encouraged to try it further. We hope that it may prove useful against certain of the trichophytons at least, perhaps in extended courses.

Fifteen additional patients were observed from whom we did not succeed in isolating a fungus. The lesions of 10 responded to the treatment in a fully satisfactory manner and those of 4 in a fairly satisfactory manner. It seems likely that a large proportion of these infections were caused by *M. felineum*, in which event such an outcome would be anticipated.

SUMMARY

A local application is presented for the treatment of tinea capitis, consisting of 2 per cent gentian violet and 10 per cent salicylic acid, dissolved in 95 per cent alcohol.

The preparation is recommended for ringworm due to microsporons of the animal type but not for that due to microsporons of the human type.

The limited results of the treatment of ringworm due to certain trichophytons were in some respects encouraging.

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ABSTRACT OF DISCUSSION

DR LESLIE M. SMITH, El Paso, Texas. Physicians are always grateful for suggestions and formulas which offer promise of shortening the course of ringworm of the scalp. A few years ago roentgen ray epilation was the standard routine treatment for such infections regardless of the causative fungus. More extensive use of the culture tube has changed this. Investigators of the subject now know that infections caused by the so-called animal microsporons tend toward spontaneous cure. Dr Spiller and his co-workers have shown that a large proportion of the cases of ringworm of the scalp seen in Galveston are cases of infection with animal microsporons. At the other end of Texas, eight or nine hundred miles away, and under different climatic conditions altogether, I think there is an even greater proportion of cases of infection with animal microsporons. My colleagues and I estimated that in well over 90 per cent of our cases of ringworm of the scalp the lesions were due to that microsporon of animal origin *M. lanosum*. I believe *M. lanosum* is identical with the organism Dr Spiller classifies as *M. felineum*. We have not done roentgen ray epilation of the scalp for, I suppose, seven or eight years.

The formula which Dr Spiller and his associates have suggested, containing a keratolytic agent and a fungicidal dye, would be beneficial in this type of infection, if any local application would. My own personal experience with this treatment, since Dr Spiller told me of his results, has been too brief to allow

accurate judgment We have treated a few patients according to Dr Spiller's directions, and on the whole our results have been satisfactory I expect to try it further

I believe the value of any treatment in these cases is enhanced by early epilation of the infected area by means of forceps It isn't necessary to epilate the entire scalp, as is done with roentgen rays, but a few hairs should be pulled out each day This certainly facilitates the cure It accomplishes the double purpose of ridding the scalp of the bulk of the infected material and of allowing better penetration of the fungicides into the follicles

Any intensification of the inflammatory process in the lesion tends to hasten the detachment and consequent removal of the hair This can be accomplished by the application of irritants, such as mercury and iodine in combination or alternately, and also in some cases by causing a focal reaction by injecting a concentrated microsporon antigen or culture filtrate I have seen the reaction occur when the antigen or filtrate was injected subcutaneously into the arm In other cases in which I haven't been able to accomplish this, I have injected the antigen or filtrate intracutaneously into the lesion and have had a flare-up I think that in some cases this hastens epilation by intensifying the inflammatory process and aids in the cure

It is well to keep in mind these various methods of treatment and to consider a combination of several methods in cases in which the infection proves resistant to routine application of the various formulas which have been used

DR W F SPILLER, Galveston, Texas Dr Smith mentioned the lanosum and the felineum They are one and the same thing We follow Dr Emmons, who visited us a while, in the use of the term felineum

Pulling out the hair is a good method, but it is quite a job, especially if the hair is not short, as there may be so many small lesions that they won't be seen That is the reason I always have the heads shaved

Dr Smith spoke of extract We have done a bit of work on extract of fungi, but of fungi of other parts of the body For a while we thought there was some virtue in the treatment with extract, but I have been thoroughly convinced that there is none, with one exception we do get some good results from treating monilia infections with an extract

Clinical Notes

FISTULAS FROM DEAD TEETH SIMULATING DERMAL EPITHELIOMA

DOUGLASS W MONTGOMERY, M D, SAN FRANCISCO

Although rarely mentioned in differential diagnosis, the mouth of a fistula may so resemble a cutaneous cancer as to deceive one into treating it as such. The following cases illustrate this fact.

REPORT OF CASES

CASE 1—Recently a man was referred to me for treatment for what was thought to be an intractable epithelioma of the chin, for which he had been previously treated unsuccessfully by another physician. At the bottom of a deep conical hollow at the tip of the chin, exactly in the place where a dimple frequently occurs, was a small ulcer resembling an epithelioma. The patient said that eight months previously it had swollen and had discharged a quantity of pus and that it had been growing larger and deeper ever since. This should have put me on the alert, but its appearance, its course and its long endurance seemed to leave no doubt of its nature. A small quantity of soft tissue resembling either granulation tissue or tissue found in epitheliomas was curetted out. The lesion was then cauterized with trichloroacetic acid and irradiated with heavily screened radium. All appeared well for a couple of weeks, and then the lesion reopened. While my associate Dr. Viecelli was examining it, he employed a probe and demonstrated a fistula leading upward and backward toward the front teeth, one of which, the left lower incisor, was found to be discolored and seemingly dead. The patient then informed us that this tooth had been injured when he was a child but that it had never troubled him. He was sent to an oral surgeon, who examined the tooth roentgenologically. It was found to be dead and was extracted. The fistula was then cleared out, and definite and prompt healing ensued.

CASE 2—Shortly afterward an elderly woman was brought to the office to be treated for what appeared to be an epithelioma of the left buccolabial fold. It was a small persistent lesion with some induration and was situated in a seborrheic region particularly apt for epitheliomatous degeneration. With my former experience fresh in mind, I examined the teeth and found the upper left bicuspid dead and a fistula leading toward it. I have not seen the patient since, but the result of proper treatment was said to have been successful.

With a fistula emanating from dead bony structure, pouting of the orifice is a well known telltale symptom. In neither case was this present. Its absence was explained by the situation of the orifices: in the man's case, at the bottom of a deep recession in the chin, and in the woman's, in an unusually deep buccolabial fold, called by humanists "the line of sorrow."

CASE 3—Pouting, however, was present and beautifully demonstrable in a little girl who was brought to me at nearly the same time as the other 2 patients. The lesion was a smooth, glistening, bright red, accurately delineated, hemispheric

papule, with a minute hole, not a mere depression, in its very top. It was situated on the anterior surface of the upper gum directly over the root of a discolored, dead-looking upper incisor. There was no doubt about the diagnosis and about the pouting in this case, and the patient's course, after extraction of the dead tooth, was the same as that of the other 2 patients.

COMMENT

The first patient, the man with the fistula opening at the tip of the chin, was by far the most interesting. That the tooth should remain without troubling for so many years and then assert itself by causing a fistula in such an unusual situation was most strange. Fortunately, I did not remove tissue for biopsy, which would have resulted in a prominent scar. As it is, he has a large, deep but rather attractive dimple.

That the condition deceived me reminds me of a saying by Anatole France, "Il faut être très sage, pour échapper les pièges de la Nature" (One has to be very wise indeed to escape the traps set by Nature).

On finding such a lesion, definitely recognizing it as the mouth of a fistula and treating it as such, one must not be too confident, for, as MacKee and Cipollaro¹ stated, long-continued inflammatory processes not infrequently give rise to cancer. Also, according to Kummer and Lang,² epitheliomas arising from fistulas of the bone are not rare, as they were able to report 44 cases. Even with the elimination of the offending tooth and the clearing out of the fistula, a cancerous process may already have begun, which later may assert itself.

1 MacKee, G. M., and Cipollaro, A. C. Cutaneous Cancer and Precancer. A Practical Monograph, New York, American Journal of Cancer, 1937, p. 85.

2 Kummer and Lang, cited in Arzt, L., and Zieler, K. Die Haut- und Geschlechtskrankheiten, Vienna, Urban & Schwarzenberg, 1935, vol. 2, p. 859.

CHROMIDROSIS

Report of a Case

MAYNARD MURRAY, M.D., CINCINNATI

Chromidrosis is a disease of unknown cause characterized by the excretion of colored sweat. Various etiologic factors have been advanced, such as menstrual disorders,¹ absorption of pigment-producing materials² and local abnormalities of pigment production.³ This disease is to be differentiated from pseudochromidrosis, which is usually caused by pigment-producing micro-organisms. In most of the reported cases the condition was localized, in the case here reported the condition was generalized. Another notable and interesting fact is that the tears of this patient also contained the pigment.

From the Department of Physiology, University of Cincinnati.

1 Barie, E. Sur un cas de chromidrose jaune, cataméniale, alternant sur les deux mains, *Ann de dermat et syph* 10:937, 1889.

2 Le Roy de Méricourt, A. Mémoire sur la chromidrose, ou chromocrinie cutanée, Paris, J. B. Baillière & fils, 1864.

3 Heidingsfeld, M. L. The Pathology of Chromidrosis, *J. A. M. A.* 39:1519 (Dec 13) 1902.

REPORT OF CASE

Mrs R F, aged 48, complained of colored perspiration which stained her clothing. The sudden onset of the condition dated back five months. The patient had passed through the menopause three years previously without any abnormal consequences. On careful questioning as to her diet and living habits, nothing of significance was obtained. No other members of her family had any similar condition.

Physical examination revealed a rather obese white woman apparently in good health, with no abnormalities except chronic bronchitis. A cholecystogram revealed a normally functioning gallbladder. The results of studies of the blood, consisting of cell counts, determination of the icteric index, a van den Bergh test and chemical examination, were essentially normal. Urinalysis gave normal results. Perspiration was induced in the patient by placing her in a hot room and keeping her hands submerged in hot water. The perspiration that exuded from her entire body, including her scalp, was golden yellow, about the color of orange peel. Tears, caused by smelling aromatic spirits of ammonia, were also golden yellow. After surgical cleansing of the skin, cultures of the perspiration gave negative results.

Omitting various pigmented foods from the diet caused no alteration in the condition. Finally, after five weeks' observation, it was suggested that the patient discontinue using face powder. Within two days the condition had subsided, and since that time, about a year ago, there has been no recurrence.

After learning the cause of the condition, the patient burned the face powder which she had been using, thus making it impossible to obtain a sample for analysis.

This case illustrates the fact that localized absorption of a dye through the skin can give rise to a generalized excretion of the dye by the sweat glands of the entire body. In this case the dye was excreted even by the tear glands.

EFFECT OF ADDING CHLOROBUTANOL TO BISMUTH SUBSALICYLATE IN OIL INJECTED INTRAMUSCULARLY

HAROLD F HOEFER, M D, NEW YORK

This study was undertaken to ascertain whether the addition of chlorobutanol to a suspension of bismuth subsalicylate in oil would produce any untoward effect when the preparation was administered by intramuscular injection. A series totaling 1,440 injections was given to 137 adult patients in the syphilologic division of the clinic under the supervision of Dr G D Astrachan.

Bismuth subsalicylate, 0.13 Gm, suspended in 1 cc of olive oil with the addition of 3 per cent chlorobutanol was used, and as a control, bismuth subsalicylate, 0.13 Gm, suspended in 1 cc of olive oil without chlorobutanol or any other addition.

Seven hundred and twenty injections were given of each preparation. Both preparations were given by the same members of the staff in the conventional manner, 2 cc being injected into the upper outer quadrant of the buttock. Each patient received an intramuscular injection of each preparation alternately once.

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University.

weekly, and no patient knew which preparation was used at a particular time. On each visit careful inquiry was made as to pain following the injection. Three complaints were elicited, two after the injection of the bismuth in oil control and one after the injection of bismuth in oil with chlorobutanol. There was no instance of severe pain.

CONCLUSION

The preparations used were equally well tolerated, and there was no undesirable effect from either.

In my series the addition of chlorobutanol did not reduce or increase local reactions or symptoms attributable to the injection.

Obituaries

CHARLES AUGUSTUS SIMPSON, M D

1882-1939

Dr Charles Augustus Simpson died suddenly of heart failure, at the age of 57, on Dec 9, 1939. Gus, as he was affectionately called by his many friends and colleagues, was head of the department of dermatology and syphilology of the George Washington University School of Medicine. He was one of the pioneers in the treatment of cancer of the skin with radium and roentgen rays. He also contributed many scientific articles on dermatology. He was connected with the staffs of the Central Dispensary and Emergency Hospital, Episcopal Hospital, Gallinger Municipal Hospital and George Washington University Hospital, Washington, D C, and had previously been on the staff of the New York Post-Graduate Medical School and Hospital, New York. Dr Simpson attended many medical meetings, and his jovial presence will be missed in the future. His death removes a prominent figure in dermatologic circles of this country.

L McC

Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

A NECROPSY SURVEY OF CARDIOVASCULAR SYPHILIS WITH PARTICULAR REFERENCE TO ITS DECREASING INCIDENCE J W WELTY, Am J M Sc **197**:782 (June) 1939

After reviewing the records of 15,000 consecutive cases in which autopsy was performed in a period of ten years, Welty concludes that syphilitic cardiovascular disease as a cause of death has decreased at least 50 per cent. This decrease is sharper than that for tuberculosis. It is believed that the decreasing incidence may be explained by modern methods of therapy. Cardiovascular syphilis was found at 7 per cent of the autopsies. There were 192 instances of aortic aneurysm, 245 of regurgitation and 632 of simple aortitis. The expected prevalence in the Negro race was found, associated with more severe involvement. The author states that fatal cardiovascular syphilis before the fifth decade is an extreme rarity in the white race.

ON THE TREATMENT OF RAYNAUD'S DISEASE WITH PAPAVERINE INTRAVENOUSLY M G MULINOS, ISRAEL SHULMAN and ISIDOR MUFSON, Am J M Sc **197** 793 (June) 1939

In the experience of the authors, treatment of Raynaud's disease with histamine iontophoresis applied to the hands and papaverine hydrochloride given intravenously led to (1) increase in the volume of the vascular bed and in the rate of blood inflow, (2) complete alleviation of the syncope, cyanosis and pain and (3) healing of trophic lesions.

HERPES ZOSTER AND ITS VISCERAL MANIFESTATIONS ELMER S GAIS and ROBERT H ABRAHAMSON, Am J M Sc **197** 817 (June) 1939

Gais and Abrahamson reviewed the records of 137 patients whose herpes zoster was severe enough to require hospitalization. Recurrence was noted in 8 cases. Adenopathy was pronounced in only 6. Bilateral zoster was observed only once, though there were 3 patients with concomitant varicelloid lesions, in 1 of whom encephalomyelitis developed. Various derangements of the central nervous system were found in 7 cases. There was an increase of the cell count in the spinal fluid in 5 of the 11 cases in which it was examined.

In 6 cases the appearance of a fiery red erythema led to a diagnosis of erysipelas on admission to the hospital.

The authors were particularly interested in 42 patients with symptoms referable to the viscera, 7 of these having pulmonary implications, 4 cardiac, 25 abdominal and 6 renal. Such symptoms are discussed with reference to errors in diagnosis and also to the possibility of organic involvement due to the virus's being transmitted centripetally along vegetative pathways.

LYNCH, St Paul

THE TREATMENT OF POSTARSPHENAMINE JAUNDICE. LOUIS J SOFFER, Am J Syph, Gonorr & Ven Dis **23**:577 (Sept) 1939

In 1 per cent of patients undergoing antisyphilitic treatment jaundice develops, with a mortality rate of from 1 to 6 per cent. Soffer stressed the value of a high carbohydrate diet as a therapeutic measure. Such diets should consist of 400 to 600 Gm of carbohydrates per day, divided into five or six feedings. In certain cases the diet should be supplemented with dextrose injected intravenously and insulin.

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given only when glycosuria is manifested. The use of cholagogues and cholaretics in the treatment of jaundice due to arsphenamine is an unsound form of therapy.

THE MALARIAL TREATMENT OF GENERAL PARESIS. RELATION OF THE HEIGHT, DURATION AND FREQUENCY OF FEVER TO THE CLINICAL AND SEROLOGIC RESULTS. ISRAEL KOPP and HARRY SOLOMON, *Am J Syph, Gonorr & Ven Dis* **23** 585 (Sept) 1939

In a group of 182 patients with dementia paralytica to whom therapeutic fever (malaria) treatment was given and whose clinical status was known, the amount of fever with temperatures of 104, 105 or 106 F and above did not make any significant statistical difference in the clinical results. The best clinical results were obtained when more than one hundred and fifty hours of fever above 100 F was experienced. Patients who were subjected to more than ten malarial paroxysms showed the best clinical results.

A distinct relation is found to exist between serologic changes and time, regardless of the maximum temperature experienced, the percentage of serologic negativity increasing with each successive year.

SULFANILAMIDE IN CHANCROID DISEASE. ROBERT G. GREENBLATT and EVERETT S. SANDERSON, *Am J Syph, Gonorr & Ven Dis* **23** 605 (Sept) 1939

The judicious use of sulfanilamide in the treatment of chancroid was found efficacious and safe in the authors' hands. Sulfanilamide proved more efficient than any of the standard methods in vogue, succeeding where vaccine therapy frequently failed.

DEATH FOLLOWING MAPHARSEN THERAPY. S. D. SIMON and A. IGLAUER, *Am J Syph, Gonorr & Ven Dis* **23** 612 (Sept) 1939

This is the first fatality to be reported as a result of antisyphilitic therapy with mapharsen. Stomatitis, anuria and death followed five injections of the drug.

A SIMPLIFIED TECHNIC FOR ADMINISTERING OLD ARSPHENAMINE. A. BENSON CANNON, *Am J Syph, Gonorr & Ven Dis* **23** 621 (Sept) 1939

Because of his conviction that old arsphenamine is the drug of choice in the treatment of early syphilis, Cannon has devised a simplified technic for administering the drug. A 1 per cent solution (0.1 Gm of arsphenamine in 10 cc of fluid) of arsphenamine properly alkalinized is given by the syringe method. A 2 per cent solution was found to be easily tolerated by children. The solution is given by injecting 3 to 5 cc at one time, pausing for twenty to thirty seconds and then injecting 3 to 5 cc again, continuing with the injections and rest intervals alternately until all the fluid is injected. The usual individual dose of arsphenamine is 0.2 to 0.4 Gm for men and 0.15 to 0.3 Gm for women.

In clinical trials of this new method, in over 1,000 cases of syphilis in all stages there were no reactions which could be attributed either to the concentration of the solution or to the method of administration. The reactions encountered under the new method were not essentially different from those encountered under the old one except that a larger proportion of them were mild and immediate and the proportion of severe delayed reactions was correspondingly smaller.

REUTER, Milwaukee

PERIARTERITIS NODOSA. ALFRED W. HARRIS, GEORGE W. LYNCH and JAMES P. O'HARA, *Arch Int Med* **63** 1163 (June) 1939

The authors add 6 examples to the 95 acceptable cases of periarteritis nodosa in the English literature. They analyzed the series for frequency of symptoms.

and signs, the most constant changes being fever, leukocytosis and albuminuria. Purpura or cutaneous nodules were each found in about 20 per cent of the cases. Various other dermatoses appeared in individual cases.

HAVERHILL FEVER. REPORT OF A CASE WITH REVIEW OF THE LITERATURE
ELLISTON FARRELL, GEORGE H. LORDI and JOSEPH VOGEL, *Arch Int Med*
64:1 (July) 1939

The authors present the clinical and bacteriologic findings in the fourteenth sporadic case of Haverhill fever to be reported. This disease, caused by infection with *Haverhillia multiformis*, is sometimes spoken of as "rat bite fever," a term which leads to confusion with sodoku, an infection with *Spirillum minus*. Both diseases may follow a rat bite, though such a history is not always obtained in the case of Haverhill fever.

Haverhill fever is accompanied by painful arthritis and is characterized by a continued remittent fever or by a periodic intermittent fever, the febrile reaction of sodoku is of the latter type. Arsenical therapy has no effect on Haverhill fever, while the effect on sodoku is specific.

Both diseases have cutaneous manifestations but must not be regarded as simple dermatologic conditions. The eruption of Haverhill fever may be confused with one of the erythemas (infectious erythema or erythema multiforme). In the case reported by the authors a maculopapular eruption was present on the extensor aspects of the legs. The eruption continued throughout the disease, leaving pigmented areas and later causing desquamation. Small petechiae were also noted and were present on the fingers as well as on the legs. The authors characterize the eruption of Haverhill fever as embolic, in contrast with the allergic nature of the eruption of sodoku.

LIMITATIONS OF BIOPSY OF STERNAL MARROW E. V. KANDEL and G. V. LEROY,
Arch Int Med 64:121 (July) 1939

Kandel and LeRoy reviewed their experience with biopsy of sternal marrow and found that it was a superfluous link in the diagnostic chain more often than it was the sole means of establishing a diagnosis. When the biopsy was diagnostic of leukemia they found no instance in which the diagnosis was not established by other clinical means. As negative evidence the biopsy of sternal marrow is of somewhat greater usefulness. The authors emphasize that if considered without other clinical data the results of this procedure can be misleading.

METASTATIC CALCIFICATION. REPORT OF TWO CASES DAVID M. GRAYZEL and
MAX LEDERER, *Arch Int Med* 64:136 (July) 1939

Grayzel and Lederer report 2 cases of metastatic calcification. In the first the condition was associated with a leukemic myelosis, in the second it complicated a normal pregnancy in an apparently healthy young woman.

The authors divide pathologic calcification into two types: the type in which the lime salts are deposited in previously diseased tissue and the type in which the salts are deposited in apparently healthy tissue. They regard as unnecessary the distinction between calcinosis universalis, with no increase of calcium in the blood, and metastatic calcification, in which there is hypercalcemia. They also regard the level of diffusible calcium as more important than the level of total calcium.

A CASE OF ARRHENOBLASTOMA WHICH SIMULATED CUSHING'S DISEASE C. KELLY
CANELO and HANS LISSER, *Endocrinology* 24:838 (June) 1939

Obesity, amenorrhea and hirsutism were noted in a patient having other characteristics of Cushing's syndrome. Because there was roentgenologic evidence of enlargement of the sella, the surgical removal of the pituitary gland was attempted,

but only fibrous tissue and atrophic pituitary cells were found. The growth of hair on the face decreased greatly in the following six months. The patient subsequently died of a tumor of the ovaries.

In speculating as to the reason for the improvement of the hypertrichosis, Canelo and Lisser state that a pituitary cyst may have been ruptured at the time of the operation. This case illustrates the difficulties in arriving at a differential diagnosis of arrhenoblastoma, adrenal cortical syndrome and Cushing's disease.

INFLUENCE OF ULTRAVIOLET IRRADIATION UPON EXCRETION OF SEX HORMONES IN THE MALE ABRAHAM MYERSON and RUDOLPH NEUSTADT, *Endocrinology* 25 7 (July) 1939

Myerson and Neustadt found that ultraviolet irradiation increases the excretion of androsterone in urine and that irradiation of the scrotum and its vicinity proves to be more effective than irradiation of other parts of the skin. Casual and incomplete observations concerning estrogens suggest that the rise in their excretion is slower, lower and more retarded than that of androgens.

URINARY EXCRETION OF ESTROGENIC SUBSTANCES AFTER ADMINISTRATION OF TESTOSTERONE PROPIONATE RALPH I. DORFMAN and JAMES B. HAMILTON, *Endocrinology* 25 33 (July) 1939

In immature monkeys the results of intramuscular injections of large amounts of testosterone propionate are suggestive of increased excretion of estrogen, indicating that some portion of the output of estrogen by normal men may be a result of the influence of androgen.

PROTECTIVE ANTIBODIES IN THE SERUM OF SYPHILITIC RABBITS THOMAS B. TURNER, *J. Exper. Med.* 69 867 (June) 1939

Turner reports a series of experimental studies which indicate that specific humoral antibodies are produced during the course of syphilitic infection in rabbits. These protective antibodies were found in the serum of rabbits resistant to reinfection.

LINCH, St. Paul

A LIST OF SUBSTANCES FOR PATCH-TESTING AND THE CONCENTRATIONS TO BE EMPLOYED ADOLPH ROSTENBERG JR. and MARION B. SULZBERGER, *J. Invest. Dermat.* 2 93 (June) 1939

A long and useful list of substances is given, with the concentration in which they may best be employed for patch tests. The list is tabulated so as to show the vehicle for the substance and the concentration to employ, and the substances are classified according to the occupation or trade in which they are encountered.

ON THE SKIN TEST IN LYMPHOGRANULOMA INGUINALE [VENEREAL LYMPHOGRANULOMA] II WILHELM FREI, *J. Invest. Dermat.* 2 119 (June) 1939

Frei states that the most common errors in the use of the cutaneous test (Frei test) for venereal lymphogranuloma result from nonspecific reactions produced by the contamination of the vaccine with living or dead bacteria. A vial with a rubber stopper having a depressed center was used to hold the vaccine instead of the previously used vial with a rubber cap. The stoppered vial with iodine as the disinfectant was tested bacteriologically and, although not completely free from contamination, was found to be superior to the capped vial with 80 per cent alcohol as the disinfectant. Because even with the strictest technique and permanent refrigeration the improved method was not entirely free from contamination, Frei prefers ampules as containers for the vaccine. He describes his own method of preparing the vaccine and performing the test. Warning is given against making

the test on patients with acute conditions (high fever or severe inflammation) until the symptoms subside. He advises that the test be avoided entirely for patients with venereal lymphogranuloma with buboes, rectal stricture or severe inflammatory or suppurative processes near the peritoneum. In the cases of anergic venereal lymphogranuloma with buboes (not the early conditions, in which before allergy is fully developed the reactions may still be negative) in which the result of a cutaneous test is persistently negative, the inverted test is suggested. In this test sterilized pus from a patient's bubo is injected into the skin of persons with proved venereal lymphogranuloma producing a positive local reaction.

PRODUCTION OF POSITIVE SEROLOGIC REACTIONS IN RABBITS AND THE SUBSEQUENT REACTIONS OF THE SEROLOGICALLY-ALTERED ANIMALS TO INOCULATION WITH SPIROCHETA PALLIDA. FREDERIC T. BECKER, *J Invest Dermat* 2:125 (June) 1939

Rytz's work of producing positive Wassermann and flocculation reactions in rabbits' blood by the injection of flocculate obtained from the serum of patients with syphilis (untreated latent and tertiary syphilis) was repeated. The flocculate consisted of syphilitic blood serum plus cholesterolized alcoholic extract of beef heart. Animals treated in this manner and then inoculated with *Spirochaeta pallida* were found to have a longer incubation period previous to showing clinical evidence of infection than did the control animals. This fact was taken to be a manifestation of altered susceptibility to syphilitic infection. The human syphilitic flocculate was thought to be definitely antigenic, because ten times the original quantity injected into the rabbit was later obtained from the same rabbit.

CLINICAL AND EXPERIMENTAL STUDY OF INTERSTITIAL KERATOSIS. JOSEPH V. KLAUDER, ELMER R. GROSS and HAROLD F. ROBERTSON, *J Invest Dermat* 2:157 (Aug) 1939

Theories and experiments relative to the cause of syphilitic interstitial keratitis are discussed. It may be caused by (a) a direct invasion by *Spirochaeta pallida*, (b) an allergic reaction or (c) a nutritional disturbance. Some of the pertinent experiments have been repeated by the authors. *S. pallida* could not be demonstrated in pieces of cornea removed from 4 patients with interstitial keratitis. There was no evidence of allergic reaction in the cornea of rabbits injected intraocularly with horse serum. Cutaneous tests with the patients' own cornea and with the cornea of a syphilitic fetus in patients with interstitial keratitis also gave negative results. Interstitial keratitis could not be produced in syphilitic rabbits by repeated trauma of the cornea.

Studies were also made on the treatment of interstitial keratitis with the application of heat, by means of the thermophore (an instrument used to heat the cornea), both experimentally on rabbits and clinically in the treatment of patients. It was observed that the temperature required to kill *S. pallida* was at least 120° F for two minutes, while the maximum temperature the cornea could tolerate with safety was 130° F for one minute. Thermophore treatment of the involved eye could not be said to influence favorably the course of the disease, nor did treatment of the uninvolved eye prevent the subsequent occurrence with interstitial keratitis.

The absorption of neoarsphenamine by the cornea, after instillation into the conjunctival sac, and the penetration of the drug into the cornea, after its intravenous administration in rabbits, were studied. No arsenic was present in the cornea after successive instillations of a 1:600 dilution of neoarsphenamine. But after six daily intravenous injections of 30 mg per kilogram of body weight of neoarsphenamine, 0.04 mg of arsenic was found in each cornea. The involved and uninvolved eyes of patients with interstitial keratitis were treated by the instillation of neoarsphenamine, but the course of the disease was not influenced.

DAVIS, Nashville, Tenn

LUPUS ERYTHEMATOSUS OF THE CONJUNCTIVA F I YOUSEFOVA and S N BOGDANOVITCH, *Ann d'ocul* **176** 27 (Jan) 1939

Lupus erythematosus of the conjunctiva is rare. In the literature accessible to the authors, only one article could be found which related to the subject.

This report concerns an adult of 23 years who came to consultation in 1935 for a bilateral ocular condition. The malady had followed an injury to the right eye three years previously, after prolonged working in the field in the sun. The palpable swelling of the right eye was followed by an eruption of spots on the cheek and lids accompanied by photophobia and tearing. The following year the left eye became similarly affected. Since that time the patient had been treated with drops and ointments without relief. On the contrary, the spots as well as the photophobia, tearing and ocular pain increased.

Considerable further detail of the general examination is given, with three photographs. The extraordinary rarity of lupus erythematosus of the conjunctiva is to be explained in part by the fact that the symptoms are not severe enough to complain of or to be brought to the attention of the ophthalmologist or the dermatologist.

McKEE, Montreal, Canada [*ARCH OPHTH*]

MULTIPLE CUTANEOUS ABSCESSSES WITH RECURRENCE IN A NURSING A BERAUD, *Arch de med d enf* **41** 736 (Nov) 1938

A girl 1 year of age suffered from multiple abscesses of the scalp. The parents had both sustained attacks of furunculosis, and the mother's blood, fortified by specific and polyvalent vaccines, was used for immunotransfusion. This method of treatment had been successfully used by the author in many previous cases, including that of a sister of the patient, but in the present instance it resulted in complete failure. After a short period of relief, a succession of abscesses appeared over the neck and body. At this point the treatment was changed and anti-staphylococcus anatoxin substituted for the hemotherapy. The amount injected was gradually increased from 0.2 to 0.7 cc. Recovery was rapid and permanent.

CALCIFIED AND MUMMIFIED EPITHELIOMAS OF THE SKIN IN CHILDREN M FEVRE, R HUEGUININ and F VELIZ PAIZ, *Arch de med d enf* **42** 73 (Feb) 1939

Epitheliomas of this type are benign in their evolution but have many unsolved features in their pathogenesis. After operating in 7 cases, the authors made an exhaustive study of tumors of the skin in young subjects. They believe these growths to be much more common than is generally considered, especially in early life, one report concerns an infant of 3 months, and six reports in the literature concern nurslings varying in age up to 6 months. The development of the epithelioma is insidious, the evolution is extremely slow and entirely free from pain, the tumor is slightly more frequent in females. The discovery of the tumor is usually accidental. The essential characteristics are great induration, adherence to the skin and total absence of involvement of the deeper tissues. The site of the tumor is practically always either the face or the neck, but cases have been reported in which the growth involved the arm or the leg. Ulceration of the skin may occur, with discharge of calcareous material. Recurrent tumors have been observed, but multiple growths are rare. A full discussion of the histologic observations, chemical characteristics and treatment follows.

A MALIGNANT TYPE OF ACRODYNIA L CAUSSADE, J WATRIN and N NEIMANN, *Arch de med d enf* **42** 91 (Feb) 1939

Up to this time, the aspect of malignancy has never been considered in the study of acrodynia. The investigations of Marquezy and Ladet have called attention to a particularly severe type of this disease in the eastern part of France. Four

cases are reported in children varying in age from 16 months to 6 years, all were similarly affected. After several weeks the benign invasion suddenly assumed alarming features, the brunt of the attack being borne by the nervous system in the form of asthenia, adynamia and unconsciousness, with corresponding changes in expression and great disturbances in the circulatory and respiratory systems. Later the digestive apparatus was attacked, but no visceral symptoms were noted in any case. Three deaths occurred in this series, and autopsy disclosed striking changes in the tissues of the brain and the sympathetic nervous system.

LIPODYSTROPHY AND LIPOMATOSIS FROM REPEATED INJECTIONS OF INSULIN P
NOBÉCOURT and P DUCAS, Arch de méd d enf 42:193 (April) 1939

A girl of 16 years in whom diabetes had developed at the age of 9 and who had received several injections of insulin daily either in the thigh or in the hip for a period of six years had at these sites, at the time of examination, small tumors with all the physical aspects of lipomas. The tumors varied in size from that of a small nut to that of an orange and were painless and elastic. The skin was streaked and bluish.

With the introduction of protamine zinc insulin, one injection daily in the arm, the tumors of the thighs rapidly disappeared, but those on the hips regressed slowly and could readily be seen a year later. Estimations of the blood cholesterol showed it to be within normal limits.

A girl of 14 who had suffered from diabetes for six years and for several years had had daily injections of insulin in the thigh presented atrophic areas as large as the palm of the hand and about 2 cm in depth. The skin was normal in appearance but could not be picked up easily and seemed to be deprived of all subcutaneous fat. These atrophic areas remained unchanged after a year, although protamine zinc insulin was substituted and different sites of injection insisted on.

A third observation, similar to the one just described, is reported concerning a girl of 18 who had been diabetic since the age of 10.

A review of the now abundant literature on this condition, the pathologic nature of which is not understood, terminates the contribution.

AMESSE, Denver [AM J DIS CHILD]

PHAGEDENIC ECTHYMA IN AN INFANT G CARDELLE, B SANTIAGO and A G
LOPEZ, Arch de med inf 7:380 (July) 1938

The authors present a case of phagedenic ecthyma in a boy aged 1 year. There was an ulcer on the hypogastrium, extending to the left lumbar region, and there were other smaller ones on the back and extremities.

Cultures showed the hemolytic streptococcus.

The spread was rapid but without much necrosis, and the general symptoms were pronounced.

Local applications of an antiseptic paste and gentian violet were used in the course of treatment. Blood transfusions were also given.

SCHLUTZ, Chicago [AM J DIS CHILD]

Society Transactions

AMERICAN DERMATOLOGICAL ASSOCIATION, Inc

FRANCIS E SENIAR, M D, *President*

FRED D WLIDMAN, M D, *Secretary*

Clinical Meeting, Monte-Bello, Quebec, Canada, May 31, 1939

Lingua Nigra Presented by DR J F BURGESS, Montreal, Canada

F M, a white woman aged 33, was first seen May 2, 1939, on account of a marked black "hairy tongue," first noticed by her in February. She was given



Fig 1 (F M) —Lingua nigra

daily doses of 100 mg of nicotinic acid by mouth, beginning on May 12. There was gradual improvement, so that at the time of her presentation, after six weeks' therapy, little trace of the condition remains.

DISCUSSION

DR ARTHUR M GRENFWOOD, Boston. At the Huntington Clinic in Boston, many cases of carcinoma of the tongue are observed, and black hairy tongues

frequently follow irradiation in these cases. The papillae become hypertrophic and secondarily infected. It may be that the patients have a deficient diet, because of the difficulty in eating.

Syphilis with Negative Serologic Changes Exfoliative Dermatitis Presented by DR DONALD S MITCHELL, Montreal, Canada (by invitation)

B B, a woman aged 20, presented an early secondary syphilitic eruption, with a positive Wassermann reaction, on Jan 26, 1939. After the third injection of neoarsphenamine, eight days after the beginning of treatment, an erythema developed. Two days after the fourth injection a generalized erythema multiforme eruption developed. This spread and became a generalized erythroderma, with temperature to 100 F. Sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) was given, and the eruption quieted. After one week, her temperature went to 104 F, with aggravation of all signs and symptoms. There were pains in the joints, headache and increase in scaliness.

A vulvar discharge, present on admission, showed no organisms, but the complement fixation test for gonococci gave strongly positive results.

Sulfanilamide was administered, with gradual subsidence of the condition.

On February 20 the Wassermann reaction was strongly positive, and on March 1 the colloidal gold reaction of the spinal fluid was 0011100000. On March 22 the Wassermann and Kahn reactions were negative, and the complement fixation test for gonococci gave a negative result. Ten days later the reactions of the spinal fluid were normal.

NOTE—Wassermann tests made in June and August were negative. Treatment with a bismuth preparation is being continued.

DISCUSSION

DR LOREN W SHAFFER, Detroit. The reversal of the serologic reactions could be accounted for on the basis of the treatment received plus the fever that developed, a protracted fever with the temperature as high as 104 F. The history of the administration of sulfanilamide brings up several problems, of which the first is the attack of erythema multiforme that the patient evidently had. The beneficial results from the use of sulfanilamide in the treatment of this condition would be explainable if there were the possibility of gonorrhea. The fever, however, that developed in this patient seven days after the use of sulfapyridine was interesting. I have been interested in this type of reaction to sulfanilamide and have an impression that in some cases it may be explainable on the basis of a ninth day erythema. One sees various types of toxic reactions following the use of sulfanilamide after a week to ten days. They are often associated with various toxic eruptions similar to those that occur after the use of arsphenamine in the treatment of syphilis. Further, arsphenamine therapy may be used after such a reaction. In this case, sulfanilamide was used after the reaction, and the fever subsided. I believe that the toxic reactions are not necessarily contraindications to the further use of sulfanilamide.

DR DUDLEY C SMITH, Charlottesville, Va. It should be mentioned that sulfanilamide itself is an agent that will cause fever. I have encountered 2 cases in which its administration was responsible for the fever. It is not known by what mechanism the reaction is produced.

It is my impression that the concomitant administration of sulfanilamide and arsphenamine increases the incidence of untoward cutaneous reactions

DR DONALD S MITCHELL, Montreal, Canada (by invitation) The patient had little in the way of treatment, only four injections of arsphenamine and four injections of a bismuth preparation Four or five months after the initial eruption the serologic reaction is still negative Probably the patient will be given routine treatment except for the arsenicals

Extensive Keloid Following Lightning Presented by DR J F BURGESS, Montreal, Canada

R M, a white boy aged 17, came to the clinic eight years ago on account of extensive nodular linear keloids on the forehead, chin and arms He had been struck with lightning about six months previously while riding his bicycle The burns from lightning had caused severe cicatricial contractures involving the joints of the elbow and wrist Special surgical measures were attempted, but owing to the vascularity of the tissue the resulting hemorrhage was controlled with great difficulty After this, roentgen therapy was instituted, followed by considerable flattening of the lesions

The patient was presented before the Atlantic Dermatological Conference in Montreal in 1932

Tertiary Syphilis Presented by DR J F BURGESS, Montreal, Canada

N F, a Greek aged 71, presents on the right leg and ankle an eruption of areas of linear and irregularly shaped atrophic scars, with pronounced peripheral pigmentation Several rather brownish infiltrated lesions at the periphery apparently represent the primary lesion The eruption has been present two years

The general condition is good except for moderate secondary anemia The Wassermann reaction of the blood is strongly positive

The histologic picture revealed a cicatricial process in the upper layers of the corium, with thinning of the epidermis Small foci of lymphocytes were scattered through this area, in some of which an occasional multinucleated giant cell was present In some places there was also a slight perivascular grouping of this infiltration

DISCUSSION

DR J F BURGESS, Montreal, Canada The only reason this case is presented is because of the areas of linear scarring which look like typical gouged-out lesions recurring in some places I suppose that one might consider that neurotic excoriations have occurred over an underlying syphilitic manifestation

DR HOWARD FOX, New York As I remember, this man had a unilateral eruption, with grouped scars on one leg and a lesion surrounded by hyperpigmentation I think the clinical signs alone are strongly in favor of a late syphilid Incidentally, the Wassermann and Kahn reactions of the blood were positive

Lupus Vulgaris Disseminatus Presented by DR DONALD S MITCHELL, Montreal, Canada (by invitation)

Mrs P, an otherwise healthy-appearing woman aged 33, in whom tuberculous cervical adenitis, scrofuloderma and lupus vulgaris developed twenty-five years

ago, following measles, presents well demarcated brownish infiltrated patches on the skin of the face, neck, shoulders and arms. Reactions to tuberculin were positive, with no evidence of tuberculosis elsewhere. Histologic examination showed a typical tuberculous structure. Treatment in the hospital and outpatient department has consisted of ultraviolet irradiation (local and general), a high vitamin and low salt diet, intravenous injections of gold sodium thiosulfate and neoarsphenamine, local injections of phenylethyl hydriocarpate and excision.



Fig 2 (Mrs P) —Lupus vulgaris disseminatus

DISCUSSION

DR MARION B SULZBERGER, New York. I should like to suggest that the diagnosis be changed in so far as the word "disseminatus" is concerned. Lupus vulgaris disseminatus is usually a different type of eruption, an exanthematous form of lupus vulgaris in which many areas of the body are affected, including the extremities. I think that the condition in this case might best be called lupus vulgaris tumidus.

Recurrent Vesicopustular Eruption on the Extremities Presented by DR J F BURGESS, Montreal, Canada

J P, a white woman aged 30, presents a vesicopustular eruption involving the palms and soles. The nails of the fingers and toes are dystrophic, with some friability of the distal parts. There is a tendency to some grouping of the eruption, especially over the heels. The total duration of the condition is one year. The general health is good, but there is a chronic infection of the tonsils. A search for fungi gave negative results.

Histologic examination showed a hyperkeratotic area of skin with several intraepidermal vesicles and microabscesses. The hyperkeratosis was flaky. The epidermis showed acanthosis and spongiosis, with fusion, some clubbing of pegs, occasional parakeratosis and a diminished granular layer. The vesicles contained a few polymorphonuclear leukocytes and lymphocytes. There was a perivascular and slight subepidermal infiltration of round cells and a few polymorphonuclear leukocytes. No eosinophils were seen.

Treatment consisted of fungicidal applications of varying kinds, soothing applications, injections of arsenic and roentgen therapy. Partial improvement resulted. In April 1939 her tonsils were removed, after which there was an immediate exacerbation of the eruption. Since then there has been little change.

Recurrent Vesicopustular Eruption on the Extremities Presented by DR J F BURGESS, Montreal, Canada

A L, a white woman aged 42, presents a grouped vesicopustular eruption on the left instep of about one year's duration.

Pertinent investigation has revealed a chronic ethmoiditis and frontal sinusitis on the right side. She had an inflammatory condition in the pelvis two years ago. Microscopic investigation on two occasions failed to reveal fungi, and cultures were negative.

Histologic examination showed a flattened epidermis, with infiltration by polymorphonuclear leukocytes. The scale was hyperkeratotic in part, with retention of nuclei and staining properties of the rete. The corium showed some infiltration of round cells and searring.

DISCUSSION ON CASES OF VESICOPUSTULAR ERUPTION

DR GEORGE C ANDREWS, New York. I was particularly interested in these 2 cases, and I should consider the conditions in both to be a bacterid. The histologic picture in both, however, is different from that in the cases that I have observed. The lesions in the 2 cases are superficial. In the latter case, that of A L, the vesicle is impetiginous and near the surface. The histologic structure is different in the 2 cases. In A L there is a notable lymphocytic infiltration underlying the impetiginous vesicular areas. In J P there is practically no inflammatory reaction at all beneath the superficial vesicles.

The first of the 2 patients presented says that she is much better now than she was last summer, when she could not stand or walk at all and the vesicles or pustules were large and painful. Since then she has been on a Sippy diet, which has cured her peptic ulcer. That may be significant. The fact that a flare-up occurred after removal of the tonsils two months ago is also interesting. Not sufficient time has elapsed to judge the effect of removal of the tonsils. If it has not already been done, I suggest an examination of the cervix, because it is possible that there might be a further focus there. I should like to know what the blood count is.

For the second patient I suggest treatment of the ethmoiditis and frontal sinusitis. It is difficult to see the tonsils without a tonsil hook, as the anterior pillar almost hides them, but there is evidence of an inflammatory reaction in the throat. Mycologic examination must also be made. I do not see any clinical or histologic signs of psoriasis in either of the patients.

DR HAROLD N COLE, Cleveland The onychomycosis in J P is significant Until the onychomycosis is taken care of, one cannot expect further clinical progress

DR SAMUEL AYRES JR, Los Angeles I think that the changes in the nails of J P, unless microscopic examination proves otherwise, are psoriatic There are rather typical stippling, thickening and piling up underneath I should like to ask if cultures have been made for fungi I think that in view of the changes in the nails the diagnosis of psoriasis ought to be considered

DR J F BURGESS, Montreal, Canada My first impression was that the condition in J P was a frankly pustular psoriasis, but, on the other hand, I was undecided about A L I felt that it was difficult indeed to make a diagnosis of pustular psoriasis on the appearance of the face alone, unless there was a coincident typical psoriasis of the body I say that because I have seen a patient at intervals for the past twelve years on account of a recurring and persistent pustular eruption on the heels, which always suggested a fungous or corneal infection, although I could not demonstrate a fungus In the last year a widespread clinically typical psoriasis has developed I therefore, with a good deal of hesitancy, made a diagnosis between a pustular bacterid of the Andrews type and pustular psoriasis

Replying to Dr Ayres' question, mycologic cultures were made, but there was no growth

Kraurosis Vulvae with Leukoplakia Presented by DR BARNEY USHER, Montreal, Canada (by invitation)

Mrs J C, aged 51, had been under observation since 1924 for a severe and intractable pruritus of the genitalia In 1934 the diagnosis of kraurosis vulvae with lichenification was made Investigation revealed nothing of significance Treatment with estrone (theelin) was of no value

In September 1934 resection of the pudendal and perineal nerves was performed by Dr A D Campbell Since the operation the pruritus has completely disappeared except for an area about the clitoris, where it is considerably diminished In that region there is persistence of mild leukoplakia The leukoplakia elsewhere has disappeared There has been no progression of the kraurosis since 1934 Senile vaginitis with leukorrhea has persisted in spite of various applications, including estradiol benzoate (progynon B) in full dosage Histologic examination showed the epidermis to be thin and the papillae few and flattened, with small rete pegs The keratin layer showed considerable thickening but in places was absent The papillary layer was increased, while the fibrillary structure was largely lost The tissue had a more or less homogeneous appearance, with scattered spindle-shaped nuclei and numerous capillary vessels Scattered throughout this zone were lymphocytes, plasma cells and eosinophils The infiltrating cells extended into deeper layers of corium, where there was also hyperplasia of the vessels with thickening of their walls

Neurodermatitis Presented by DR BARNEY USHER, Montreal, Canada (by invitation)

Mrs A K, aged 50, was observed in 1935 with a silver dollar-sized plaque of neurodermatitis involving the upper and outer aspects of the left labium majus This had been present for two years prior to observation Chemical examination of the blood gave negative results

Histologic examination showed great hypertrophy of the epidermis, with elongation of the rete pegs The zona granulosa was practically absent, and there was superficial parakeratosis throughout the papillary zone Scattered throughout the epidermis there was infiltration of lymphocytes and polymorphonuclear leuko-

cytes There was a general hyperemia of the papillary zone and some slight edema There was also in the papillary zone some pigmented chromatophores, although there was no excessive pigment in the basal layer

Resection of the perineal and pudendal nerves was performed by Dr A D Campbell in June 1936, and the patient has remained well

Leukoplakia Vulvae Presented by DR BARNEY USHER, Montreal, Canada (by invitation)

Mrs M, aged 60, suffered for ten years from leukoplakia surrounding the clitoris, associated with severe pruritus Investigation revealed a normal pelvis and a normal amount of blood sugar Histologic examination showed decided hyperkeratinization and hyperplasia of the squamous cells Prolongation of the interpapillary epithelium was marked In some areas of the hyperplastic squamous epithelium there were accumulations of round cells Some of these were hyperchromatic, while others were vesicular They varied little in size and shape Below the epithelium there were collections of similar cells in a hyalinized fibrous stroma In places the stroma extended into the epithelium as finger-like projections The cells in these did not differ remarkably from those apparently cut off in areas of the epithelium The vessels were dilated and thin walled

Resection of the sensory nerves of the perineum (Dr G J Streat) in January 1938 was performed, with almost complete subsidence of the pruritus Great improvement in the leukoplakia, at times complete disappearance, was observed

DISCUSSION ON CASES OF LESIONS OF THE VULVA

DR LOUIS A BRUNSTING, Rochester, Minn I think the condition in the case of Mrs J C is an example of true kraurosis vulvae, with perhaps a suspicion of telangectasia and atrophy with actinodermatitis I was interested in examining the patient's tongue to find that it shows marginal atrophy Instances have been reported of generalized smoothing of the mucous membranes of the mouth and vulva In the gynecologic literature some patients with this condition are reported to have improved under the administration of hydrochloric acid and cod liver oil I suggest in this case that surgical excision of the vulva be considered if there is extension of the condition

DR HAROLD N COLE, Cleveland I have recently had the opportunity of following several cases of kraurosis vulvae, in 1 of which the condition was extensive The patients were given intramuscular injections of estrone (theelin) once a week (2,000 to 5,000 units), and the results have been remarkable I have observed results from resection or excision of the areas of kraurosis, and it is my impression that one can get fully as good results from estrone (theelin) alone

DR HENRY D NILES, New York According to the description, the lesion is on the left labium majus All I was able to find was an apparently atrophic patch on the right thigh and nothing on the labium majus

DR BARNEY USHER, Montreal, Canada (by invitation) Any scar is the result of the removal of biopsy specimens Both Mrs J C and Mrs A K received injections of estrogenic substance, one estrone (theelin) and one estradiol benzoate progynon B, but with no results An interesting feature in the case of Mrs M is that a year ago she had a $\frac{1}{2}$ inch (1.3 cm) thickened area of leukoplakia She now has almost complete relief from symptoms, with almost complete subsidence of the leukoplakia The same holds true for Mrs J C, who obtained almost complete relief from pruritus, certainly more than enough to warrant further interference The operation was done under spinal anesthesia, with no effect on the patient Relief was almost immediate One patient was followed for four years, another for five years All symptoms have disappeared, and the patients have remained fairly well

Atopic Dermatitis. Presented by DR J F BURGESS, Montreal, Canada

V St P, a white woman aged 37, shows a thickened, lichenified exudative and inflammatory eruption on the face, neck, upper part of the chest and back, cubital fossae and posterior aspects of the thighs. There are numerous excoriations. The eruption has been present for ten years, with some remissions during the first year of her illness. The general health has been good. There are no abnormal metabolic observations, and roentgenographic and special examination of the nose, throat, teeth, gallbladder and generative organs gave negative results.

Extensive cutaneous tests for protein showed a decided reaction to silk and dog hair (there had been a dog in her house for ten years). A decided reaction to silk material was obtained by applying it with moisture at the site of a linear scratch. A piece of the same silk applied to the unbroken skin under an occlusive dressing failed to cause a reaction in twenty-four hours.

Contact with silk has been removed, without any change in her eruption. Contact with dogs has not been entirely eliminated. A high vitamin diet and ample doses of capsules containing vitamins A, B, C, D and G have caused considerable improvement but have not resulted in cure.

DISCUSSION

DR WILLIAM H GOECKERMAN, Los Angeles. In my experience with atopic eczema and neurodermatitis, I cannot recall any instance in which treatment with the conventional methods has ever given satisfactory permanent results. I should like to bring up a point which I emphasized three years ago at the meeting of this association, when I received further encouragement in my point of view from the discussion by others. I think that in a definite subgroup of patients with this syndrome the disease is the result of a deficient diet. I cannot select these patients by objective appearance but have to be guided by the history. The condition does not occur necessarily among poverty-stricken people. This type of patient usually comes from a family in which the father is active and at home little and the mother leads the life of a club woman who leaves the care of the children to servants. There is an abundance of good food, and the meals which are provided are usually well balanced, but the child, often precocious, does not eat what is put on the table. I now have 3 cases in which this peculiar cutaneous picture, which I am beginning to look on as an entity, is present. With an adequate diet the response was striking and seemingly permanent. The exact element in which the food is deficient in these cases I do not know. For the present I can only suggest that a fully adequate diet be given when such a condition is suspected. One patient under my observation has gone for four years without a recurrence. At the time I started to give her this treatment she was 17 years old. I do not have enough cases of this type for study to evaluate this particular feature of the subgroup, and therefore I should like to call emphatic attention to it so that dermatologists who have a larger amount of material at their command will give it a trial. The best that I can suggest today is that dermatologists go into the history of their patients most carefully in order to ferret out a deficiency in the diet.

DR MARION B SULZBERGER, New York. I agree with Dr Goeckerman concerning the difficulty of proving what role allergens play in the production of the clinical manifestations of the atopic cutaneous disease. It is particularly difficult to prove whether or not the removal of allergens benefits the patients and, if so, what percentage of them is benefited. I think that in some of these cases, particularly when more youthful persons are affected, allergens without question play a definite role. I also think that removal of specific factors from the food or environment of an adult rarely effects a cure or even gives great relief. The situation is much like that with asthma. In at least 50 per cent of the persons with asthma removal of allergens does not effect relief. However, the role of allergens in this case is easily seen. The patient gave reactions, when the skin was tested not only with com-

mercial silk allergen but also with material from one of her own silk dresses. Moreover, the wearing of certain of her silk dresses has produced clinical exacerbations. In addition, a piece of silk dress moistened with potassium hydroxide and applied to normal skin without scratching led to the appearance of a large wheal and flare. I think that there is a definite demonstration that there can be transepidermal penetration of silk allergen and that the wearing of silk is under certain conditions inclined to produce wheals, itching and a tendency to scratch in this woman. It is, of course, obvious that this is not the whole story, even in this case, and that not only silk but many other things cause this patient to itch and scratch.

DR J HARPER BLAISDELI, Boston. I should like to point out some difficulties in removing offending allergens in such cases. The patient was wearing silk stockings. I do not think it is sufficient to tell a woman not to wear a silk dress if at home she exposes herself to a silk dress worn by her sister. This patient is sensitive to dogs and has been in contact with a dog for many years. I have always found it difficult to cleanse a home from the dander and hair of a dog. Removal of the dog is not sufficient, a thorough cleansing of the premises is also necessary. One must take into account not only the exposure of the patient to substances which he wears but also his contact with what other members of the family wear.

DR GEORGE C ANDREWS, New York. I should like to suggest that this patient try two or three things. One is that she use a nasal filter. These in a measure protect against pollens and other inhalants. Some of her trouble may be from inhalants as well as from substances with which her skin comes in contact. I have used nasal filters with some success in cases of allergic eczema due to inhalants. I also suggest passive transfer tests. One should test for reactions to several food materials, to silk and to dog hair. She might also be desensitized, by injections, if she can be, to substances to which she reacts positively. These measures probably will not cure her but should make her trouble less annoying.

DR J F BURGESS, Montreal, Canada. In the past year and a half I have had a number of patients with atopic eczema who have improved under treatment with large doses of mixed vitamins. One of these, a young girl, had a persistent lichenified eczema of the face and neck, and a good many tests were done on her prior to the time I saw her. They showed that she was sensitive to a number of different allergens. I had the impression that she was getting little vitamin C in her diet, and so for one year I have given her large doses of ascorbic acid by mouth. Since that time not only has her eruption entirely disappeared, but also her attacks of nervous irritation. I think she belongs in the group of patients whom Dr Goeckerman referred to.

DR JOHN ANTHONY GAMMEL, Cleveland. One cause of the difficulties physicians encounter in approaching cases of atopic eczema by way of allergens is the great number of possibilities to be considered. There are cutaneous tests for a few hundred allergens but there are many more possibilities which one cannot detect unless one spends days with the patient. Suppose one finds out that he is sensitive to silk and to certain feathers. At the same time he may be allergic to a dozen unsuspected and unusual substances for which it is impractical to test. The known factors are eliminated, but the eczema persists because the other, unidentified causes have not been removed.

Danlos' Syndrome Presented by Dr BARNEY USHER, Montreal, Canada (by invitation)

E C, a girl aged 7 years, presents hyperelasticity of the skin, hyperlaxity of the joints and a doughy feel of the skin. Scarred atrophic areas are present on the elbows, knees and forehead, associated with hemorrhage following slight injury

The condition has been present since birth. The only pathologic change revealed by laboratory examination was increased fragility of the red blood cells.

Histologic examination showed changes in the fibers of elastic tissue. There were reduplication, fragmentation and condensation of the fibers, with a moderate degree of alteration of the collagen bundles.

DISCUSSION

DR RICHARD S. WEISS, St. Louis. Dr. Usher was fortunate in getting an example of this peculiar syndrome—hyperelasticity of the skin, hyperlaxity of the joints and pseudotumors. The condition is not as marked as some I have observed in St. Louis. In some cases the hyperelasticity of the skin is so prominent that the skin can be pulled out 6 or 8 inches (15 to 20 cm). The microscopic changes were consistent with those I have observed.

Case for Diagnosis (Phenolphthalein Pigmentation?) Presented by DR DONALD S. MITCHELL, Montreal, Canada (by invitation)

S. S., a healthy boy aged 15 months, is presented with a generalized macular to confluent light brown pigmentation which developed nine months ago. The child had been fretful, and the mother had given him $\frac{1}{2}$ tablet of "ex-lax." The following day a generalized eruption appeared, which was followed by the present eruption. It is less prominent on the face and upper part of the trunk than when first seen, six months ago. About two weeks ago the child showed a few papulourticarial lesions scattered on the trunk and face. The lesions do not show wheals after rubbing them.

Biopsy has not been permitted. The results of scrapings were negative for fungi. There has been intermittent use of a mild ointment containing salicylic acid.

DISCUSSION

DR E. WILLIAM ABRAMOWITZ, New York. Tissue from the affected areas should be examined microscopically for the presence of mast cells to exclude urticaria pigmentosa. The question of an eruption from phenolphthalein or urticaria pigmentosa came up in connection with a case recently presented by Dr. Frank Fraser (*ARCH. DERMAT. & SYPH.* 40:512 [Sept.] 1939) before the New York Dermatological Society. Several biopsies showed only scattered mast cells, not sufficient to warrant labeling the condition urticaria pigmentosa. Phenolphthalein and other drugs were ruled out as a cause. Another recent instance of an acquired pigmentation over the eyelid brought up the question of a phenolphthalein eruption or argyria. A drug eruption was finally excluded. Dr. Satenstein, after a study of a cutaneous section in the latter instance, thought that the condition might be a nevus of the mast cell variety. Andrews in his textbook on cutaneous diseases reports on a nursing infant with a fixed eruption thought to be due to phenolphthalein ingested by the mother, however, as it is known that free phenolphthalein is not excreted in mothers' milk (Fantus, B., and Dyniewicz, J. M. *Am. J. Digest. Dis. & Nutrition* 3:184 [May] 1936), it is questionable whether the eruption was due to the drug. I have never seen an eruption from phenolphthalein in an infant. There is no other report of such a case in the literature.

DR HOWARD FOX, New York. At first glance the eruption would appear to be urticaria pigmentosa, but, as Dr. Abramowitz has pointed out, there are several points against this diagnosis. In the first place, there has been no formation of wheals on rubbing the lesion, and I failed to observe any today. In the second place the lesions tend to coalesce and form fairly large patches, a tendency I do not recall having observed in urticaria pigmentosa. In that disease the lesions, whether small or large, are entirely discrete. In the third place, there is definite history of ingestion of a preparation containing phenolphthalein. Dr. Abramowitz and I should be able to recognize an eruption due to phenolphthalein as he and I

independently described the first case. He is entitled to the chief credit, as he proved the diagnosis by subsequently giving the patient more of the drug (Abramowitz, E. W. *J. Cutan. Dis.* 36:11 [Jan] 1918).

DR ROBERT L. GILMAN, Philadelphia. Regardless of the diagnosis in the case of this particular infant, I believe that the pigmentation is excessive either way. I noted too that the mother has decided chloasma.

DR HARTHER L. KEIM, Detroit. It might be informative if Dr. Mitchell could have the child brought back and give him a small amount of phenolphthalein.

Xanthomatosis (Schuller-Christian Disease) Presented by Dr. Donald S. Mitchell, Montreal, Canada (by invitation).

In A. S., an undernourished-appearing child of 12 years, a fairly profuse eruption of small yellowish papules developed on the face, trunk and arms three years ago. There had been polydipsia, polyuria and loss of weight for several months previous to the eruption.

Investigation showed a urinary output of 10,000 to 12,000 cc daily, with a specific gravity of 1.000 to 1.002. There was 211 mg of cholesterol per hundred cubic centimeters of blood. A roentgenogram of the skull showed an area of rarefaction in the right parietal region, "which did not have the usual appearance associated with xanthoma," according to the interpretation. All other examinations gave normal results. Histologic examination showed typical xanthoma, with considerable inflammatory infiltrate.

DISCUSSION

DR FRED D. WEIDMAN, Philadelphia. I doubt that there is a sufficiency of items to establish this condition as Schuller-Christian disease. There is no history of exophthalmos or jaundice. The only item in support is the fact that there was some prenatal defect. In the literature there is a report of a case (Herzenberg, H. *The Skeletal Form of Niemann-Pick Disease*, *Vuchow's Arch f. path. Anat.* 269:614, 1928) in which there were cholesterosis and defects in the membranous bones, which was regarded as a case of multiple myelomatosis with a superimposed xanthomatosis. In sections of tissue from the patient presented here the histologic picture is unusual indeed. The cells are remarkably large, clear and definitely outlined. The nuclei are apparently huge. When I first saw the sections I thought of the case of neurocytoma which Drs. Montgomery and O'Leary presented two years ago. I suggest that studies be prosecuted further to determine whether the conditions in the 2 cases could be the same or, if not, to determine whether this condition is possibly a disease fundamentally of the blood-forming tissue. Some special primitive type of cell may be at fault, perhaps a plasmoblast. I was not satisfied with the foaminess of these cells. The cholesterol of the blood measured only 211 mg per hundred cubic centimeters, which is not particularly high.

DR PAUL A. O'LEARY, Rochester, Minn. I agree that there are some clinical features in this case that resemble those in the case of neurocytoma or neuroganglioneoma that Dr. Hamilton Montgomery and I reported several years ago. The patient does not present any evidence of Schuller-Christian disease at this time but rather presents the picture of multiple xanthomatosis or disseminated xanthomatosis. The finding of normal values for fat and lipid in the blood does not exclude the possibility of xanthomatosis, because in the disseminated form of xanthomatosis normal values have been obtained on numerous occasions. I favor a diagnosis of disseminated xanthomatosis and urge further study of the histologic material in an effort to establish the diagnosis. There have been varying degrees of success in the treatment of patients with this condition by placing them on rigid ketogenic diets.

DR DONALD S. MITCHELL, Montreal, Canada (by invitation). In looking up the literature I found a suggestive idea in an extensive article (Warkany, J., and

Mitchell, A G Diabetes Insipidus in Children A Critical Review of Etiology, Diagnosis, and Treatment, with Report of Four Cases, *Am. J. Dis Child* 57:603-666 [March] 1939) on types of diabetes insipidus classified according to associated conditions One type was that associated with xanthoma which, the authors stated, usually constitutes part of the Hand-Schuller-Christian syndrome

Hypodermic Sarcoid Presented by DR J F BURGESS, Montreal, Canada

L L L, a white man, presents a large bluish red inflammatory tumor, the size of an orange, on the inner aspect of the middle third of the left thigh According to his history, he first noticed the lesion eight months ago, and since that time it has progressively enlarged His general health is good He said that tuberculosis of the kidney developed in his daughter in 1913, after the drinking of nonpasteurized milk, and that some years later she had a tuberculous osteitis of the hip, with a discharging sinus which has never healed and which is draining at the present time His reaction to tuberculin with dilutions of 1 1,000, 1 10,000 and 1 1,000,000 was strongly positive

Histologic examination showed numerous rather well demarcated areas containing many lymphocytes and epithelioid cells in the upper part of the cutis, while deeper down there were nests of epithelioid cells and some giant cell formation

Suggestions as to treatment are requested

NOTE—Total excision was performed shortly after the meeting

DISCUSSION

DR PAUL E BECHET, New York The tumor-like growth on the left thigh is raised and vegetating It occurs on the site of a biopsy wound done several months ago I should under these circumstances suspect malignancy I should suggest surgical excision of the tumor mass, as though it were definitely malignant, and then a histologic examination of the excised material

DR GEORGE C ANDREWS, New York The clinical appearance of the lesion is not typical of sarcoid, and although I am no specialist in histology, certainly I thought that the microscopic appearance was more typical of mycosis fungoides I should like to suggest that the condition is the d'emblee type of mycosis fungoides The clinical appearance of the plum-colored lesion suggests some lymphoblastic process, and the short duration of the tumor growth, I think, is uncommon in sarcoid I suggest roentgen therapy

Hypodermic Sarcoid Presented by DR J F BURGESS, Montreal, Canada

S, a white man aged about 45, presents brownish red, rather glazed crescentic and oval thickened inflammatory areas on the forehead and forearms, which appeared three months ago This is his third attack of exactly the same clinical process, the first having been in 1929 and the second in 1932, which lasted two years His case was investigated during the second attack, and the aforementioned diagnosis was made No foci of infection were found after a thorough check-up, and roentgenograms of the bones of the hands and feet were normal There was no history of the ingestion of drugs The blood smear was normal The Mantoux reaction was negative with dilutions of 1 1,000, 1 10,000 and 1 1,000,000 The Wassermann reaction of the blood was normal Numerous forms of treatment were tried, and the eruption eventually cleared up with gold therapy Further investigations during the present flare-up gave similar results

Histologic examination in April 1939 showed extensive inflammatory changes in the upper half of the corium The epidermis was irregularly acanthotic, with some spongiosis and vesiculation The corium showed a generalized infiltrate of small round cells, with numbers of plasma cells The blood vessels were dilated

and perhaps increased in number. A second section, taken one month later, showed a similar picture, with an infiltrate made up almost wholly of lymphocytes and a few polymorphonuclear leukocytes.

DISCUSSION

DR ERWIN P. ZEISLER, Chicago. I think that because of definite nodules in the ears and the glabella and other nodular lesions, I should rule out leprosy. Stains for acid-fast bacilli should be made.

DR RICHARD S. WEISS, St. Louis. When I first looked at this patient, I thought of leprosy, but on examining more carefully I think that could be ruled out. There is no enlargement of the ulnar nerve, and there are no areas of anesthesia. When I studied further, however, it seemed to me that he presented leukemia of the skin, and I thought the observations on the histologic section bore that out. I have encountered 1 or 2 cases in which the ears were affected just as were the areas about the eyebrows. I think the condition in this case may turn out to be a leukemia.



Fig 3 (S) —Hypodermic sarcoid

DR F. E. SENEAR, Chicago. I at first had the same feeling that Dr. Zeisler expressed, that this was a case of leprosy, and, unlike Dr. Wise, I thought that there was definite enlargement of the ulnar nerve on the left side. On considering the remainder of the clinical picture, however, I did not feel that anything else could be determined to support that diagnosis. I think Dr. Zeisler suggested that the patient be thoroughly investigated from that standpoint.

DR J. F. BURGESS, Montreal, Canada. I shall certainly investigate the condition as to the possibility of its being leprosy. I shall also have further examinations of the blood done from the standpoint of possible leukemia.

NOTE—Studies have revealed no evidence of leprosy, and complete blood counts and smears have shown no suggestion of leukemia.

Atopic Eczema with Bilateral Cataract Presented by DR DONALD S. MITCHELL, Montreal, Canada (by invitation)

A. H., a man aged 22, presents erythematous, squamous, lichenified and at times exudative eczema of most of the body surface, especially that of the face and neck and over the flexors.

There was a generalized eruption from the age of 3 to 7 years, and the present condition has existed since he was 15. Asthma has been present since the patient was 10 years old, which is worse in the winter and at night but better when he smokes cigarets. His vision was good in both eyes prior to the spring of 1937, but at that time vision in the left eye became poor. In December 1937 the right eye became affected suddenly, and the vision of the left eye then seemed to be improved.

His tonsils and adenoids were removed in 1932. The sinuses are clear. Cutaneous tests and a general investigation showed no abnormal results. Treatment has been symptomatic.

DISCUSSION

DR LOUIS A. BRUNSTING, Rochester, Minn. Cataract is held to be a rare complication of atopic dermatitis, but if careful examination is made with a slit lamp evidence of incipient cataract can sometimes be detected in the form of postcapsular opacities even before there are clinical symptoms of blurring of vision. At the clinic 35 cases of cataract in association with atopic dermatitis have now been observed. In 8 of the cases there was no record of treatment with roentgen rays. This is important from a medicolegal standpoint, as roentgen rays have been incriminated as a factor in the production of cataracts. In most instances in our experience the condition has occurred in patients in their twenties, the youngest patient known to have the condition being 15 (possibly there was one aged 8 years). In the ophthalmologic literature there is mention of a form of hypersensitivity to lens protein. Other theories, such as Dr Goeckerman's of a form of avitaminosis, deserve careful scrutiny, but so far no satisfactory explanation has been advanced to account for the formation of cataracts in these cases.

DR JACOB HYAMS SWARTZ, Boston. In a group of patients with atopic dermatitis at the Massachusetts General Hospital there were about 10 with cataracts, and the ophthalmologic report was "deficiency type of cataract." As Dr Brunsting has stated, the age in these cases is usually 15 or above. I believe that perhaps restriction of the diet from infancy on may be the causative agent.

Mycosis Fungoides Presented by DR BARNEY B. USHER, Montreal, Canada (by invitation)

U. L., a man aged 38, was first seen one year ago for fleeting attacks of dermatitis. Large plaques of scaly dermatitis soon appeared with paroxysms of severe pruritus, which gradually became infiltrated and indurated with tumorous development. Sites of predilection were the lateral aspects of the trunk and upper extremities. There was no adenopathy. Hematologic examination showed moderate lymphocytosis and moderate monocytosis and a slight increase in the rate of sedimentation. Histologic examination showed isolated columns and masses of cells, lying in the upper layers of the corium and extending downward into the deeper layers. These aggregates of cells were remarkable because of their variegated appearance. Within such aggregates large numbers of eosinophilic polymorphonuclear leukocytes were encountered. There were considerable numbers of endothelial cells, small numbers of lymphocytes and considerable numbers of pale cells with vesicular nuclei that in many respects resembled endothelioid cells except that the cytoplasm was slightly different. Small numbers of fibroblasts were encountered, and a few capillaries were seen in such aggregates of tissue. No giant cells of any type were encountered except that in some situations there were agglomerations of endothelioid cells which give pseudogiant forms. There was no necrosis or exudation. The masses of exudate were irregular in size and varied in distribution, the major portion being in the upper layers of the corium but extending in fairly well defined masses into the deeper layers. Cellular detritus was not prominent in these collections of cells.

Administration of sulfanilamide, 30 to 60 grains (2 to 4 Gm.) daily for two months, resulted in almost complete healing of the condition. There was a recur-

rence when the drug was stopped. No improvement was noted under sulfapyridine therapy but rather a return to the original state. There was improvement when sulfanilamide therapy was resumed.

Eczema Seborrhoeicum Presented by DR DONALD S MITCHELL, Montreal, Canada (by invitation)

J P, a man aged 38, foreign born and of the long unemployed laboring type, presents a chronic recurrent erythematous and exudative, and at times psoriasiform, eruption on the scalp, face, ears, eyelids and flexures, of six years' duration. There has been an intermittent folliculitis of the bearded region and furunculosis of various parts of the body.

Yeastlike forms were observed on direct examination on one occasion. Cultures have yielded only staphylococci. Complete physical and laboratory examinations have shown nothing abnormal. Histologic examination showed decided acanthosis with long tongue-like projections. Along a hair, at the surface and extending down along it a short distance, there was a polymorphonuclear leukocytic reaction. Surrounding this and about the follicles and blood vessels there was an intense infiltrate of plasma and round cells. In the interstitial tissue there was less cellular reaction and some connective tissue reaction.

Treatment with various ointments and lotions, dyes, roentgen rays, staphylococcus toxoid and foreign protein has been only irregularly helpful.

DISCUSSION

DR E WILLIAM ABRAMOWITZ, New York. I understand from Dr Usher that a congo red test was done a year ago and the result was negative. I suggest that it be repeated because the lesions on the legs resemble a local amyloidosis of the skin.

DR J H MITCHELL, Chicago. In this type of case I am not able to arrive at any opinion without a great deal of work in the way of cultures and microscopic studies. The numerous follicular infections rather suggest a staphylococcal infection. Of course, the staphylococcus and the streptococcus possibly coexist. The lesions about the canal of the right ear are suggestive of a streptococcal infection, but the lesions in the axillae are hardly of the "open book" type. The fissuring is typical on the soles.

DR SAMUEL AYRES JR, Los Angeles. This case closely resembles several I have encountered in the past two or three years, in which there have been a follicular pustular infection, blepharitis and a seborrheic type of lesion in the axillae, face and scalp and sometimes in the genitocrural region. At times the lesions on the face are definitely follicular, resembling sycosis vulgaris, and at other times they look like lupus erythematosus. Because of the fact that the seborrheic and pustular lesions would at times give place to erythematous lesions on the face suggestive of lupus erythematosus, gold therapy was used in several cases and fairly good results were apparently achieved. I think the condition in the case being presented is most recalcitrant. There is undoubtedly something in the background besides a follicular infection, even though that factor has not been encountered in this type of case.

DR E WILLIAM ABRAMOWITZ, New York. I think that we have all had trouble in treating this type of dermatosis. I would suggest 30 per cent sulfur in petrolatum to be applied once or twice daily. I have found this to be effective.

Kaposi's Sarcoma Presented by DR DONALD S MITCHELL, Montreal, Canada (by invitation)

L L, a thick-set Italian aged 44, presents thickened infiltrated inflammatory plaques and nodules of ten years' duration on the ears, nose, hands and feet.

The first histologic examination, made four years ago, showed a patchy lymphocytic infiltration scattered through the corium, with more about the vessels and glandular structures.

Section made a year later showed typical angiosarcoma. Injections of an arsenical compound have been used. The lesions have been kept under control.

mainly by high voltage roentgen therapy In 1938 an acute abscess developed on the foot, with fever, necessitating hospital care for two months, after which many of the lesions flattened considerably and some seemed to have entirely disappeared

DISCUSSION

DR HIRAM E MILLER, San Francisco A patient was presented at the meeting of the American Dermatological Association in San Francisco ten or more years ago with many lesions of angiosarcoma of Kaposi on his feet, hands and ears About seven years ago a severe streptococcic infection of the upper part of the arm



Fig 4 (B H) —Pemphigus (Senear-Usher syndrome)

developed, with fever (temperature of 106 to 107 F) for a considerable time Two months later the lesions of Kaposi's sarcoma began to disappear, and in five months they were entirely gone That was six years ago, and he is still entirely free of the disease

Pemphigus (Senear-Usher Syndrome) Presented by DR BARNEY USHER, Montreal, Canada (by invitation)

B H, a man aged 33, presents greasy scales in the scalp, demarcated crusted inflammatory lesions on the cheeks and nose and crusted areas on the back and axillas with bullous formation predominating The duration of the eruption is eighteen months Otherwise his condition is normal

Histologic examination of an early lesion showed a small corner of a bulla, the roof being mostly missing. The base showed ragged epidermis varying in thickness and missing in places. There was edema of the papillary part of the corium and the epidermis, with little vascular dilatation and polymorphonuclear exudate about the vessels, some of the cells streaming into the epidermis. The middle and lower parts of the corium showed little change except some exudate of round cells about the fixed structures. A section of an older lesion showed acanthosis with a diminished granular layer and only a little scaling. There was an infiltrate, intense about the vessels, in the papillary portion of the corium, made up chiefly of lymphocytes, with an occasional polymorphonuclear leukocyte and plasma cell. At one site the epidermis was thinned and flattened, with cellular infiltrate beneath. The lower part of the corium showed only moderate edema.

Treatment consisted of injections of a gold preparation, a high vitamin diet, administration of mixed vitamins by mouth and local application of sulfur and tar. No improvement was noted.

DISCUSSION

DR OLIVER S. ORMSBY, Chicago. My impression is that the condition is pemphigus, but not the erythematodes variety. In this form of pemphigus the eruption resembles lupus erythematosus of the nose and cheeks, while on the chest and back the lesions resemble seborrheic eczema and in addition there are bullous lesions of the pemphigus type. The lesions therefore present the clinical features of lupus erythematosus, seborrheic eczema and pemphigus. The patient had a rather generalized eruption consisting of flaccid bullae together with an exfoliative dermatitis, which is characteristic of the foliaceus variety of pemphigus rather than the erythematodes type.

DR BARNEY USHER, Montreal, Canada (by invitation). In the initial phase of the disease, the patient presented what appeared to some of those who saw him to be seborrhea of the scalp, with scaling and greasiness. Then a bat wing-shaped lesion developed on the bridge of the nose, which persisted for some months, and in the last few months there has been a gradual development of a bullous eruption on the body. The initial lesion was that of seborrheic eczema, impetiginous in parts. Only in the past few months has the pemphigus foliaceus eruption developed.

NOTE.—The patient died two weeks after the presentation, apparently of a septicemia. Staphylococci were obtained from the blood at necropsy.

Prurigo (Hebra) Presented by DR BARNEY USHER, Montreal, Canada (by invitation).

N. E., a man aged 57, born in Galicia, presented a papulourticarial lichenified eruption on all the extremities and lower half of the trunk. The older lesions are intensely lichenified and in places nodular. There are increasing pigmentation and intense pruritus. The condition was first noted eight years ago, since which time he has been on a "relief" diet, decidedly deficient in vitamins. Beggar's psychologic neurosis was diagnosed by the neurologist. Chemical examination of the blood and hematologic examination gave normal results. There were no foci of infection, and the basal metabolic rate was normal. Histologic examination showed a surface covered by keratinized stratified squamous epithelium in which only a few minute foci of parakeratosis were seen. In one place in the epidermis there was a small vesicle filled with partially degenerated epithelium. The papillary layer of the cutis was edematous, showed a slight proliferation of connective tissue cells and was focally infiltrated by lymphocytes and round cells. The deeper layers of the cutis were moderately edematous, and the edema was most evident in the perivascular region. In the perivascular areas infiltrations of round cells and lymphocytes were observed, but no plasma cells or eosinophils. The deeper layers showed a number

of sweat glands, which were not remarkable. Sections stained with congo red showed no amyloid. No change was noted after intradermal injections of congo red.

Treatment consisted of administration of a high vitamin diet and calcium, ultra-violet irradiation, roentgen therapy and application of Unna's paste. No change was noted in consequence.

Radiodermatitis Cellular Keloid? Presented by DR J F BURGESS, Montreal, Canada

N McL, a white woman aged 30, had roentgen ray therapy in 1926 for hypertrichosis of the chin. She was seen first in 1930, when there were ulceration on each side of the chin and marginal telangiectasia and atrophy. These conditions healed after eight months. In 1937 she presented a tumor the size of a marble on the left side of the chin, which was thought to be an epithelioma but was not ulcerated. It was desiccated, and radium was applied. Healing resulted, but three

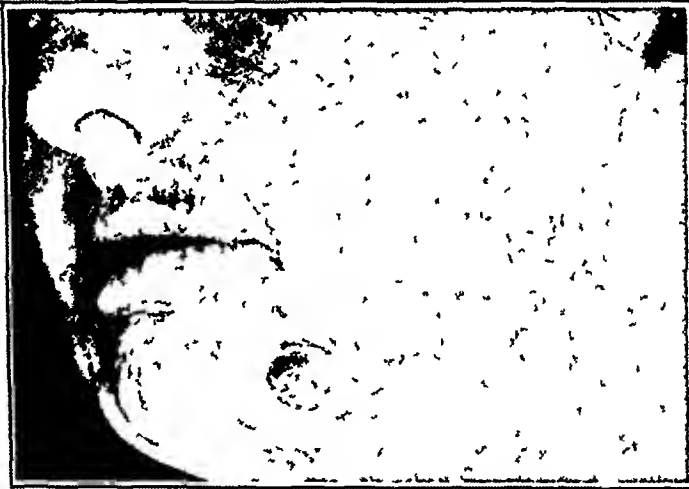


Fig 5 (N McL) —Roentgen ray sarcoma

months later there was a recurrence. A biopsy was performed at that time, and the following report was made:

The histologic section showed a cellular fibrous tissue covered by a layer of epidermis devoid of papillae. The cells were spindle shaped with intervening collagen which in places was edematous. There were a few endothelium-lined vascular spaces, which did not contain any blood. At the base of the section there was a small area of more normal zona reticularis. There was an overgrowth of cellular fibrous tissue on the upper part of the skin, covered directly by epidermis devoid of papillae.

In July 1938 the tumor, the size of a tangerine, was removed surgically, and skin was grafted. Recurrence was again seen at about the same area. It was thought that the tumor was attached to the bone. A roentgenogram of the mandible showed some decalcified areas in the region underlying the growth. The tumor was again desiccated and destroyed down to the surface of the bone in February 1939, with a recurrence within two months.

The case is presented for an opinion as to diagnosis and further form of treatment.

DISCUSSION

DR ERWIN P ZEISLER, Chicago I should like to offer the diagnosis of sarcoma I think the rapidity of recurrence is inconsistent with the diagnosis of keloid The histologic observations also could be interpreted as those of a neurogenic sarcoma The problem of therapy is a difficult one This type of sarcoma recurs unless widely removed surgically, and it is radioresistant I suggest interstitial radium therapy

DR J F BURGESS, Montreal, Canada The histologic diagnosis was benign cellular tumor After following the case for a time and noting the great tendency of the condition to recur, I feel that it must be considered clinically a malignant growth I propose to have the patient observed by a competent surgeon, with a view to widespread and total removal

NOTE—Shortly after the meeting the patient was admitted to the hospital, wide excision was performed and the operation was followed by electrocoagulation, which involved the bone, after stripping of the periosteum, and resulted in partial necrosis of the bone Subsequent histologic studies showed that while in some areas keloidal change predominated, in others the sarcomatous nature of the growth was revealed The pathologist's diagnosis was roentgen ray sarcoma In September a wide area of bone sloughed away In October three separate pea-sized reddish brown papules appeared about the original site of the growth

Hemolytic Jaundice with Ulceration of the Skin Presented by DR J J MCGOVERN, Westmount, Quebec, Canada (by invitation)

S, a white man aged 23, has been under observation for two years on account of recurrent indolent multiple ulcers of both legs which have been refractory to treatment

Investigation showed a negative Wassermann reaction, a basal metabolic rate of -1 per cent, with a normal roentgen picture of the blood vessels of the legs The hemogram of September 1938 showed the sedimentation rate to be moderately accelerated, with a moderate shift to the left of neutrophils There was evidence of a toxic condition

In May 1939 there was a slight macrocytic hypochromic anemia, with a decided leukocytic shift to the left The type of anemia with abnormal fragility of the cells corresponds with a clinical diagnosis of hemolytic jaundice

A barium sulfate enema showed that the splenic flexure was displaced medially by the spleen, which was enlarged

A histologic section was made of a portion of skin in the center of which was an ulcer with necrotic inflammatory exudate on the surface The epidermis on either side was normal and dipped down slightly at the margin The base of the ulcer was hemorrhagic, the hemorrhage having separated the tissue which appeared as bundles of connective tissue carrying blood vessels, most of which showed endothelial hypertrophy and about which were proliferation of large endothelial cells and infiltration with lymphocytes and plasma cells Beneath this the area of dense scar tissue was also infiltrated with lymphocytes, plasma cells and a few eosinophils, particularly about the blood vessels Some of the arteries showed thickening of the walls and compression of the lumen Some showed hyaline degeneration Scattered throughout were phagocytes containing blood pigment The lesion appeared to be a chronic ulcer showing marked fibrosis at its base and extensive recent hemorrhage

The treatment recommended was splenectomy

DISCUSSION

DR DUDLEY C SMITH, Charlottesville, Va I should like to suggest the possibility of sickle cell anemia in this case Routine blood smears may not show the sickle-shaped or crescentic red cells, but they can be demonstrated in a hanging drop of blood This condition and other kindred diseases of the blood may cause chronic ulcers A few cases have been reported in the white race

DR C L CUMMER, Cleveland I should like to ask whether the patient has shown icterus at any time I do not note any jaundice today

DR J J MCGOVERN, Westmount, Quebec, Canada (by invitation) The patient for the past two years has suffered from chronic ulcers of the lower part of the legs The ulcers would improve while he was at rest in the hospital with the legs raised, but when he was allowed on his feet they broke out again Investigations showed that they were not varicose, tuberculous or syphilitic ulcers Attention was directed to an article (Taylor, E S Chronic Ulcer of the Leg Associated with Congenital Hemolytic Jaundice, *J A M A* 112:1574 [April 22] 1939) that gave us a clue The hemogram on two occasions showed increased fragility of the red cells The report of the van den Bergh test on two occasions was direct, delayed, indirect, positive 2 units and 15 units, respectively The bleeding time was one and three-tenths seconds The histologic diagnosis was nonspecific chronic ulcer A barium sulfate enema revealed the splenic flexure displaced toward the midline by the spleen, which was thought to be enlarged An icteroid tint of the scleras was observed two or three times By the process of elimination, the conclusion is forced that the condition is a chronic ulcer of the leg due to hemolytic jaundice

There have been altogether, according to the article in *The Journal*, 17 cases reported in the literature, mostly in Germany and in Scandinavian countries The treatment recommended is splenectomy

DR GEORGE M LEWIS, New York The punched-cut appearance of these ulcers and the history the patient gives of itching and traumatization due to it, with the absence of palatal reflexes, would suggest dermatitis factitia

DR J J MCGOVERN, Westmount, Quebec, Canada (by invitation) In answer to the question as to whether the lesions could be self inflicted, I may say that some time ago the leg was put in a boot of Unna's paste (hard paste of zinc oxide N F), which covered the ulcer completely When the boot was removed, three or four weeks later, the ulcer had increased considerably in size This, I feel, rules out the possibility of factitial dermatitis

DR F E SENEAR, Chicago A replica of this picture of ulcer of the leg was recently observed in a patient with sickle cell anemia and again during the past month in a patient with Cooley's anemia, associated with extreme fragility of the red cells In a recent issue of *The Journal of the American Medical Association* attention was called to the type of ulcer of the leg shown today by Dr McGovern in association with Cooley's anemia It is obvious that if one considers anemia as an explanation for old chronic ulcers on the leg, particularly in young persons, the opportunity of studying a most interesting new group in dermatology will be provided

DR FRED D WEIDMAN, Philadelphia I agree that there is a possibility of factitial dermatitis However, Dr Ketron will shortly read a paper before the American Dermatological Association, Inc (Ketron, L W Cutaneous Manifestations of Periarteritis Nodosa, *ARCH DERMAT & SYPH* 40:929 [Dec] 1939) on periarteritis nodosa, and I invite the members to keep in mind the picture of this patient at that time In the sections there is evidence of definite vasculitis and perivasculitis The condition under discussion is not true periarteritis nodosa, but I think that some of the members may have read a recent article on polyarteritis nodosa describing conditions which resemble this one The fleeting jaundice may be due to toxic hemolysis, it was stated in the history that there was evidence of a toxic condition I do not know whether this man has vasculitis or not, but in any event the possibility of periarteritis should be investigated The age of the patient is against this diagnosis, since patients generally do not live as long as this man has

DR F E SENEAR, Chicago I was referring particularly to the type of ulcer shown in the photograph in Dr McGovern's case and not to the small lesions disseminated over the legs generally

NEW ENGLAND DERMATOLOGICAL SOCIETY

FREDERICK S BURNS, M D, *President*BERNARD APPEL, M D, *Secretary**Boston, Feb 8, 1939***Myositis Ossificans** Presented by DR BERNARD APPEL, Boston

In 1924 this patient, a 37 year old Negro choreman, had a crushing injury of his left thigh, with avulsion of skin and muscle tissue. The area healed with formation of a keloidal scar. About three months ago the center of the scar broke down, and an ulcer resulted, from which spicules of bone protruded.

The patient repeatedly showed a positive Hinton reaction and is now receiving active antisyphilitic therapy. There is no clinical evidence of either early or late active syphilis.

Examination shows an ulcerated area 2 inches (5 cm) in diameter in the middle of the lateral aspect of the left thigh. This is located in the center of a long band of keloidal scar tissue extending from the upper part of the thigh to a point several inches below the knee. There are many spicules of bone protruding from the ulcerated area.

Roentgen examination showed typical myositis ossificans.

DISCUSSION

DR WILLIAM P BOARDMAN, Boston. Two or three questions arise in this case. The man probably has syphilis. Whether the present condition has anything to do with the syphilis or not is a question, but treatment does not seem to have modified it in the short time that he has been treated. The other thing is that the area in which the scar is broken down and the bony spicules are found is that in which he received roentgen and radium therapy some years ago, which healed the original traumatic ulcer. Whether that has anything to do with the formation of these bony spicules I do not know. A roentgenogram of the knee was taken, which did not show any such spicules lower in the scar. This would seem to indicate that the roentgen rays and radium had something to do with the origin of this trouble.

In regard to treatment, it seems that wide excision of that part of the scar might be of benefit, although if the process is going on and gradually involving the whole scar, excision of that part of it would do no good.

DR FRANCIS M THURMON, Boston. I should like to suggest fever therapy as supplementary to the antisyphilitic treatment.

Mycosis Fungoides Presented by DR C GUY LANE, Boston

Six years ago this 62 year old man noticed mild scaling and pruritus of his legs which persisted in spite of therapy and gradually spread to involve the entire body. Approximately eight months ago severe pruritus developed and was accompanied by formation of nodules, which increased in size, ulcerated and became necrotic. There is now generalized involvement of scaling, tan-brown and deep red plaques of various shapes and configurations. Scattered over the trunk are crescent-shaped deep brown raised scars. On the abdomen, left thigh and left knee five tumors are present, varying from 2 to 6 cm in diameter, which are fungating and the centers of which are necrotic.

The white blood cell count was 9,000 per cubic millimeter, with polymorphonuclears 76 per cent, lymphocytes 16 per cent, mononuclears 4 per cent and eosinophils 4 per cent.

DISCUSSION

DR E W ABRAMOWITZ, New York (by invitation). I think it is a case of fairly typical granulomatous disease.

DR BERNARD APPEL, Boston I should like to call attention to a report recently submitted of the apparent cure of mycosis fungoides in 5 or 6 of 8 cases by intramuscular injections of chaulmoogra oil esters and to state that I have tried such therapy in 1 case. Unfortunately, the patient had too advanced a condition and died of bronchial pneumonia before I had a chance to give her many injections, but there was apparently slight improvement in the symptoms after six injections. I think chaulmoogra oil may be of some value.

Actinomycosis Presented by DR C GUY LANE, Boston

This 39 year old man has had a dermatitis and swelling of the entire right side of his face since June 1938. At that time he noticed a swelling of the right cheek, which within three days thereafter reached its present size. A week after the onset small pustules appeared over the surface. The only growth noticed since is a slight downward enlargement. The patient is a roofer. He does not come in contact with animals or with hay, but he puts nails in his mouth and has been having his teeth extracted during his present illness.

The swelling at present extends upward to the zygomatic arch, impinges on the loose tissue of the lower lid and extends backward over the ramus of the mandible and into the submaxillary area. There is woody induration, and the overlying skin is taut and deep brown. Scattered over the surface are many pustules and areas of scar retraction.

Pus obtained by aspiration from one small fluctuant area contained many small round yellowish granules which were identified as actinomycotic and which are growing anaerobically. Microscopic examination showed chronic inflammation. One positive Hinton reaction, four negative Hinton reactions and one negative Laughlin reaction were reported after examination of the blood.

Treatment has consisted of thymol, 15 Gm, three times a day on two of every three days. The superficial pustules have disappeared and infiltration around the eye has subsided, but there is no change in the greater portion of the lesions.

DISCUSSION

DR J H SWARTZ, Boston When the case was first presented at one of the staff meetings, I was opposed to the diagnosis of actinomycosis because of the firmness of the lesions, and it looked to me more as though there were involvement of the parotid gland, but after a while, as the lesions were dressed, I saw definite discharging abscesses, and by Dr Ray's microscopic demonstration the diagnosis was definitely established. I feel that in this case ethyl iodide would be of value.

A Case for Diagnosis (Lupus Erythematosus? Lichen Planus?) Presented by DR MAURICE MYER TOLMAN, Boston

This 28 year old man is exposed to the sun a great deal. Two or three years ago lesions appeared on his lips, but there was no definite relation to sunburn. These have been slowly increasing in size, and at present there are red, scaly leukoplakia-like lesions on both lips, with an elevated circinate border which shows definite stippling above and just beyond the vermilion border. The tip of the nose seems erythematous, and there is greater than normal prominence of the follicles.

Treatment has consisted of intramuscular bismuth subsalicylate.

DISCUSSION

DR AUSTIN W CHEEVER, Boston I favor a diagnosis of lupus erythematosus. It does not seem to me that the lesions inside the mouth are consistent with a diagnosis of lichen planus. I am wondering, since most of them are on the right side of the mouth, whether the gold teeth on that side have something to do with

the process The pattern inside the mouth is rectangular and fits pretty well the impressions made by the teeth

DR FRANCIS M THURMON, Boston I should like to suggest the diagnosis of a resistant, slowly growing benign epithelioma

DR J H SWARTZ, Boston I think, since the diagnosis has been offered, I favor lichen planus, particularly for the lesion on the lower lip The lesions are discrete As one looks at them closely, they have an umbilication, and the color on the lower lip is suggestive of lichen planus The lesion on the upper lip, I admit, is not as definite and would fit in perhaps with the picture of lupus erythematosus In correlation with a study of each lesion, the primary lesions and the development of the process, I believe that microscopic examination would probably show lichen planus

DR C GUY LANE, Boston It seemed to me, in looking at these lesions carefully through the lens, that there was enough evidence to warrant a diagnosis of lichen planus If one examines the lower border of the lesion on the lower lip, there are definite small annular lesions They have a little pearly ring and a little umbilication which shows well with the lens, and I think part of the lesion has a suggested linear arrangement which compares well with what one sees as Wickham's striae in other lesions of lichen planus The same holds true of the lesion in the middle of the upper lip, particularly above the upper limit of the vermilion border, where there is a definite annular lesion, again with a fine whitish or pinkish line around the periphery I think that in this lesion also there are areas characteristic of Wickham's striae

Lupus Erythematosus Presented by DR C GUY LANE, Boston

Three months ago this 21 year old woman noticed a small brown raised area on her left cheek, it slowly spread peripherally, leaving the center shining and clear No treatment was given, and several other such areas appeared spontaneously New and old lesions are now present on both cheeks The new lesions consist of bean-sized brown maculopapules the border of which blends into the normal skin The oldest lesions consist of circular areas approximately 3 cm in diameter with slightly raised borders and smooth, shining atrophic centers in which are seen many dilated, plugged follicles

Microscopic examination suggested lupus erythematosus

DISCUSSION

DR J H SWARTZ, Boston The appearance of the pathologic section is not against the diagnosis of leprosy Also, in one part of the slide the picture is consistent with lupus erythematosus

DR JOHN GODWIN DOWNING, Boston I do not think the clinical picture is that of lupus erythematosus First, notice the character of the circular lesions The ulnar nerve is definitely thickened The patient was born in Russia and has not been in the United States many years One cannot dismiss the suggestion of searching for Hansen's bacillus and making sure that there is no possibility of leprosy

Pemphigus Presented by DR C GUY LANE, Boston

This 57 year old woman has had chronic lacrimation, a feeling of "mucus in her throat" and recurrent small blisters on her hands and face for three years One month before admission to the hospital she had a sensation as of a foreign body in her right eye

The right eye shows considerable symblepharon, especially of the outer canthus and the lower cul-de-sac The upper lid shows scarring, with considerable thickening and conjunctivitis The posterior portion of the palate shows linear scarring,

the soft palate and the tonsillar pillars are scarred and adherent to the posterior pharyngeal wall, so that there is only a 0.5 cm opening from the nasopharynx. There are no cutaneous lesions.

Examination of the sinuses shows thickened mucosa.

Treatment has consisted of injections of pontocaine hydrochloride. Symptomatic improvement has been obtained.

DISCUSSION

DR E W ABRAMOWITZ, New York (by invitation) Dr J V Klauder has had a great deal of experience, and he presented before the Philadelphia Dermatological Society (*ARCH DERMAT & SYPH* 38:988 [Dec] 1938) a series of cases with the diagnosis of essential shrinking of the eye. I think this case falls into that category. I don't know whether the dermatologists will accept this condition as pemphigus in the absence of the lesions that one usually looks for on the body and in the mouth when no conjunctival shrinkage is present, but time will tell.

I remember seeing a condition of this kind in a young boy some years ago (Cohen, M., and Sulzberger, M. B. Essential Shrinkage of the Conjunctiva in a Case of Probable Epidermolysis Bullosa Dystrophica, *Arch Ophthalm* 13:374 [March] 1935). The patient had shrinkage of one eye, and it was suggested that he be given potassium iodide. This is exceedingly dangerous. The boy, of course, had a reaction in the involved eye. I do not consider it advisable to use such treatment, but it is interesting to consider, especially with the lesions developing in the back of the throat. I have never seen anything like that before, and I should not think of suggesting the diagnosis of pemphigus unless essential shrinkage of the eye is the same thing as what dermatologists call pemphigus.

DR E LAWRENCE OLIVER, Boston. Within the last ten years, in consultation with the physicians of the Eye and Ear Infirmary, I have seen a number of patients with this type of process. One of them had cutaneous lesions (bullae), but most of them showed simply this condition of the eyes, with severe conjunctival adhesions. I think that conjunctival adhesions, especially on the lower lid, are suggestive of pemphigus and that when such lesions are accompanied with oral lesions one can make a diagnosis of pemphigus. I had a private patient who had this condition for three or four years before anything showed on the skin, but later she had an extensive bullous eruption all over the body.

DR JOHN GODWIN DOWNING, Boston. About one month ago I was asked to see a baby at St Elizabeth's Hospital. The baby was born by normal delivery, and at birth bullous lesions were noticed on both lips. When the baby cried bullous lesions were noticed on the tongue and on the lower gingiva. When the nurse applied oil on the outer aspect of the arm during the usual cleaning of the skin a bullous lesion arose there, later a series of them appeared on the body, face and extremities. These gradually quieted down. Cultures of material from the lesions were sterile. The child is still living. Most of the lesions in the mouth and most of those on the body have disappeared, but there is still an occasional one on the extremities. The interesting part is that on the right leg, just below the patella, there is a foveated scar at the site of one of the lesions. The first diagnosis was pemphigus neonatorum, but the condition is now believed to have been epidermolysis bullosa.

DR C GUY LANE, Boston. I wish to point out that this patient has had other lesions on the skin which were consistent with pemphigus. I think it is proper also to call attention to the results of consultation with oculists and laryngologists. Several specialists in diseases of the eye have seen the patient and have made a diagnosis of pemphigus. Dr H P Mosher saw her and emphasized the fact that similar lesions in the throat may be produced by pemphigus or syphilis.

Scar of Oriental Sore. Presented by DR C GUY LANE, Boston.

At the age of 18 months this 35 year old Turkish woman had a boil on her right cheek, which came to a head. The eye was not swollen, although persons

living in her neighborhood with similar lesions did have swollen eyes. The lesion was treated with poultices and incision. The patient lived in Turkey until she was 10 years of age. On the right cheek, below the lateral half of the right eye, there is a rather depressed white scar about 2 cm in diameter, with a ragged edge. There is no evidence of activity.

DISCUSSION

DR MAURICE J STRAUSS, New Haven, Conn. I know almost nothing about Aleppo boils, but this scar has an unusual appearance. I should like to ask whether this is typical of the scar left by an Aleppo boil or whether that diagnosis was made simply because the lesion occurred in Turkey.

DR E LAWRENCE OLIVER, Boston. The patient comes from Harpoot, and she says her mother tells her that practically all of the people there have this disease at some time, usually in childhood. I think the statistics will show that fully 90 per cent have it. I think it is a characteristic scar. When I was in Turkey, many years ago, I saw a large number of persons on the street who had similar scars on the face.

Spontaneous Necrotic Dermatitis (Hemolytic Streptococcus) Presented by DR C GUY LANE, Boston

This 52 year old woman has had arthritis for the past thirty-four years. At the age of 12 she had tuberculous adenitis. In 1914 her tonsils and adenoids were removed, and there was a submucous resection for a discharge. She had a positive Wassermann reaction in 1917, but all the reactions have been negative since. She was admitted to the hospital on Oct 14, 1938. Fifteen months previously a "pimple" had appeared on her right breast. At onset this had a blue-black appearance, and it soon broke down to form an ulcer. This healed in a few weeks, and another lesion appeared on the left breast in the same manner as the first. This did not heal well and spread peripherally to involve nearly the entire left breast. Under therapy in the hospital it healed in three months. Since then she has had these lesions to a lesser extent in various places. The patient describes two types of lesions: one a small red pinpoint area which appears and disappears equally rapidly, the other blue-black lesions which go on to form small blisters filled with black fluid, which may break down to form small ulcers or go on to form large ulcers, as already mentioned. She has had these on her elbows, buttocks and hands. Three weeks prior to her admission to the hospital one formed on the right ankle, over the internal malleolus. This progressed to ulceration and caused the patient to come to the hospital.

She presents large scarred areas on both breasts and the right internal malleolus and small, sharply circumscribed scars on both buttocks.

The patient was tested with various vaccines and showed a specific necrotic reaction which reduplicated the spontaneous lesions when hemolytic streptococcus vaccine was given intradermally. This occurred in a dilution as high as 1:1,000. Controls did not react in this manner. The patient was also tested with non-hemolytic streptococci, *Staphylococcus aureus*, *Staphylococcus toxoid*, plain broth, *Bacillus coli*, *Streptococcus viridans*, typhoid vaccine and tuberculin. To these various vaccines her reaction did not vary from the normal. Intradermal injection of beta hemolytic streptococcus extract and of the protein and carbohydrate fractions of the streptococcus elicited no abnormal reaction.

Microscopic examination of one of the purpuric areas a few hours old showed "thrombosis of small vessels in the corium, just below the epidermis."

Microscopic examination of an intact necrotic nodule showed "intact epithelium and an area of acute inflammation below it."

DISCUSSION

DR L CAPLAN (by invitation). The patient is hypersensitive to hemolytic streptococci. With Dr Champ Lyons' help two fractions were obtained, the car-

bohydrate fraction and the protein fraction, and unfortunately she did not show in response to either fraction any hypersensitivity greater than the controls. Dr Lyons said that there are about five fractions in hemolytic streptococci, but those treating her were not able to obtain the other three fractions. She was tested with a nonhemolytic streptococcus and the various other streptococci, and she showed hypersensitivity to hemolytic streptococci with a solution as high as 1:1,000.

A Case for Diagnosis (Atrophia Cutis Maculosa?) Presented by Dr JOSEPH MULLER, Worcester, Mass

About two and one-half years ago the mother of this 15 year old school girl noticed oval white spots on the girl's arms and shoulders. She has never been seriously ill. The menses started at the age of 11, and the periods are regular. There are round and oval lesions from 1 to 2 cm in diameter in which the skin is thin, depigmented and dry. Other lesions of the same size appear in groups. For the first two months they are slightly raised and pink. Afterward they change to the picture just described.

Treatment has consisted of administration of thyroid, of iron and solution of potassium arsenite U S P, without benefit.

Microscopic examination shows enormous thickening of the corium, which, as measured from the sections, is fully 6 mm in thickness. The epidermis is thin, being two cells thick in one portion of a section and in other places varying from three to four, five, six or eight cells in thickness. There are few changes in the epidermis other than slight hyperkeratosis, atrophy, shortening of the rete cones and some atrophy of the appendages. Beneath the epidermis and in the superficial parts of the corium there is a zone fully 1 mm wide in which the collagenous fibers are swollen and appear fragmented and gnarled. Between them there is a fine deposit of pink-staining material. The blood vessels are infrequent in this zone, and those present are surrounded by thin collars of lymphocytes and a few scattered plasma cells. In the deeper part of the corium the collagenous fibers are broad, heavy and enlaced. Only a few fat cells are seen, and these surround the atrophic coils of sweat glands and groups of sebaceous glands. A few fat cells also border the blood vessels. Few nuclei are present in the mass of collagenous tissue. These changes are histologically in keeping with the atrophy of the skin described by Jadassohn under the term "anetoderma erythematodes" and otherwise known as atrophia cutis idiopathica maculosa.

DISCUSSION

DR MAURICE J STRAUSS, New Haven, Conn. This may be a case of benign tumor-like new growths of Schweninger and Buzzi.

DR E WILLIAM ABRAMOWITZ, New York (by invitation). I should like to second Dr Strauss's suggestion. I don't think the picture is entirely the classic one of that disease, but I think that with the other lesions present, even though they do not have the buttonhole depression, it is a form of that condition.

There is another point that I want to speak about, which may be a slight digression. I transilluminated these lesions, they looked like little sebaceous cysts, and they transilluminated very clearly. I have been doing some work with transillumination and examination of lesions and benign cutaneous growths with a useful and inexpensive little instrument which has been of great help to me, especially in connection with melanoma. I am using the term "melanoma" to designate the dark blue pigmented lesion that one ordinarily suspects of being malignant. In transilluminating the various growths I find that cysts and, for instance, this particular lesion are superficial epitheliomas and the light goes right through them, whereas in xanthoma for instance, hard fibroid tissue will come out rather cloudy. The most important use of transillumination is in the case

of a pigmented growth which has been tampered with, to determine whether the growth should be excised and, if so, to what extent Transillumination in such a case sometimes shows little opaque dots far beyond the pigmented lesions, indicating that the melanoma is malignant

DR E MYLES STANDISH, Hartford, Conn There are two distinct phases of this disease On the back of this patient the lesions are new, definite, tumor-like, hard and raised, whereas on the anterior axillary borders there are distinct button-hole-like lesions, about two or three on each side, with definite atrophy I agree with Dr Strauss's diagnosis

DR ELLWOOD C WEISE, Bridgeport, Conn It is my impression that the tumors of Schweninger-Buzzi disease at first may appear red or may have a bluish tint At first they are firm Later, after they undergo further atrophy, some of them possess this soft feeling On palpation one gets the impression of a herniation through what appears to be a ring at the base of the growth

I should like to hear from some one on that point (color and consistency at onset), because it is my recollection that the lesions are firm at first and become soft only after the atrophy has progressed

DR MAURICE J STRAUSS, New Haven, Conn Perhaps I should not have been so brief, but my reason for suggesting this diagnosis was the presence of lesions in both stages, the tumor-like new growths on the back and the lesions over the front of the arms, which the patient told me were the original lesions and which have undergone an atrophic change

DR JOSEPH MULLER, Worcester, Mass The oldest lesions are on the neck, they show cigaret-paper-like structure New lesions at this time are few A good many of the spots which one sees today appeared two months ago At that time they were slightly raised There was no bluish color They are gradually fading out and regressing to the level of the skin I performed a biopsy at that time A histologic study was made, and the slides were presented today There is no change in the epidermis—no change anywhere except in the collagen fibers, which show decided swelling No abnormal cells which would suggest a tumor are visible, or at least I could not see any I think I shall stick to the diagnosis of atrophica cutis idiopathica maculosa

A Case for Diagnosis (Lupus Erythematosus? Besnier-Boeck-Schauman Disease?) Presented by DR WILLIAM P BOARDMAN, Boston

Two weeks before admission this 15 year old student noticed redness of her hands Three weeks after that onset destructive lesions appeared on her fingers and an "eruption" on her face She has had scars on the lower parts of her legs for years Since onset of the dermatosis there have been a loss of appetite and a loss of 8 pounds (3.6 Kg) in weight

On admission there were erythematous infiltrations of the flexor and lateral aspects of the fingers The extremities were cold One week later there appeared crusted, keratotic depressed lesions on the fingers at their distal portion, more prominent on the index fingers All the lesions were pea sized, irregularly circular and pale There was a pink macular lesion on the left cheek, with fine scaling, about 1.5 cm in diameter There were about twelve small papular lesions of the nose and the right cheek, occurring in clusters, and one shallow depressed scar near the right ala nasae There were several old cyanotic scars on the lower parts of both legs, macular, round and about 3 cm in diameter

DISCUSSION

DR ELLWOOD C WEISE, Bridgeport, Conn I suggest the diagnosis of Hutchinson's chilblain lupus, because of the nodular character of the lesions, the central crusting and umbilication and the scars, also the more or less acrocyanotic condition of the hands, all of which go to form the picture of that condition In lupus erythematosus the individual lesions form patches covering a larger area

DR J H SWARTZ, Boston I favor the diagnosis of lupus erythematosus In simple discoid lupus erythematosus there is decided vasomotor stability of the hernia-like lesions, some of which have definite thrombosis of the vessels, and also the necrotic lesions which are present in this case This particular patient shows some of these vascular manifestations plus typical lesions of lupus erythematosus on the face The slide also, I think, is suggestive of lupus erythematosus

DR ELLWOOD C WEISE, Bridgeport, Conn The condition can be put to a therapeutic test It has been rather striking to me to see such conditions respond rapidly to cod liver oil given internally and to local ultraviolet ray therapy It is my opinion that if this condition is lupus erythematosus response to such simple treatment would not be evident, in fact, such measures might be contraindicated Keeping the hands and fingers of the patient warm with woolen gloves is desirable

A Case for Diagnosis (Atopic Dermatitis? Bacterial Dermatitis?) Presented by DR ARTHUR M GREENWOOD, Boston

This 19 year old boy has had eczema since infancy, which has usually been confined to the flexor surfaces There have been periodic exacerbations and remissions with no relation to habitat, climate or season Two years ago this condition became progressively worse, spreading for five or six months, until practically the entire body was involved It has remained more or less unchanged In youth the patient found by experience that eggs made his condition worse, but in the past few years this type of food has seemed to make no difference The patient's father has a similar cutaneous disease and was similarly troubled in his youth A paternal aunt has hay fever The patient frequently has large open fissures back of the auricles, such as are often associated with bacterial dermatitis

There is lichenification of the back of the neck and of the antecubital and popliteal fossae, extending from which is a rather uniform scaly erythroderma involving the entire face, the neck, the upper extremities, the upper part of the trunk and the thighs

DISCUSSION

DR JOSEPH MULLER, Worcester, Mass I looked at the patient and found that there are two types of lesions One type involves the cubital fossae and the back of the neck The other type is diffuse inflammation of the face and front of the neck The appearance of the first type is characteristic of atopic eczema The long duration of the patient's trouble is consistent with that The erythematous condition of the face may be of bacterial origin If it is, I think it is superimposed on atopic eczema, as I am sure that the basic trouble is atopic The treatment ought to be based on careful cutaneous tests or on the results of elimination diets For the erythematous lesions I do not know anything better than the usual local applications

DR ARTHUR M GREENWOOD, Boston This is typical of a number of extremely persistent eruptions for which local treatment is futile as far as my experience is concerned This young man has had the most expert treatment since the trouble began He has seen numerous dermatologists, and everything possible has been done He has lived under the best possible conditions, and nothing has helped him except perhaps temporarily His eruption is apparently independent of climate, of surroundings and of season A certain amount of cutaneous testing has been done, with negative results More complete tests will, however, be made There is one thing that seems to me possibly to point to a cause for part of his trouble At various times he has had fissuring of the skin, particularly back of the ears, which in my experience is not associated with uncomplicated dermatitis from external irritants With the idea that this might be due to bacterial infections I asked Dr Champ Lyons to see him He does not feel that the streptococcus is a factor Dr Ray has made intradermal tests, and the patient gives a decided

reaction to oidiomycin. It is possible that a yeast is the secondary invader. My theory is that he has a sensitization to external irritants plus an infection with a yeast and possibly with a streptococcus. I hoped some one would have some suggestions as to treatment.

DR J H SWARTZ, Boston. I think there are two notable factors in this case. First, season and climate do not affect the condition, and second, the distribution of the lesions and the history of infantile eczema classify it with what is called at present atopic dermatitis. In this type of involvement, as past experience has shown, although cutaneous tests give positive results, elimination or removal of the so-called allergic agents does not effect an improvement. I fully agree with Dr Greenwood that there is a bacterial or yeastlike factor, but I think it is secondary.

DR FRANCIS M THURMON, Boston. Because of the urticarial phase I should like to make a therapeutic suggestion. Give the patient potassium chloride in 5 grain (0.32 Gm) doses three times a day for five days.

DR J H SWARTZ, Boston. I have tried potassium chloride in such cases at the Beth Israel Hospital. My experience with the drug has not been as satisfactory as that reported by others who have used it for both urticaria and atopic dermatitis. Perhaps my experience has been too limited to evaluate it.

DR JOSEPH MULLER, Worcester, Mass. The fact that the swelling subsided after the injection of epinephrine does not prove its bacterial origin. In urticaria, which is definitely an allergic manifestation, injection of epinephrine produces good results. I think the fact that all the cutaneous tests gave negative results proves nothing, especially as they were performed by an untrained technician. I make all my cutaneous tests myself, and I obtained negative or false positive results on several occasions. If, from the clinical picture, I am positive that I am dealing with a cutaneous allergy, I resort to elimination diets. I clearly remember 1 case in which by doing so I was able to clear up an eruption of many years' duration. Two foods were causing trouble which elicited persistently negative reactions, and three others which elicited positive reactions on repeated examinations proved to be harmless to the patient.

DR BERNARD APPEL, Boston. I should like to make a suggestion about further diagnostic procedures. I questioned this young man about tests. He said he had had a great many scratch tests but no patch tests. I suggest that he be given contact tests, or patch tests, with some of the substances with which he may come in contact, including flower extracts, perfumes and common materials within his environment. Recently I have made scratch tests on a patient with certain substances and obtained what I interpreted as a negative reaction, subsequently the patient was given patch tests with the same substance, and a positive reaction was obtained. Elimination of that substance resulted in prompt clinical improvement.

I feel that in these types of atopic dermatitis patch tests are as important as scratch tests.

Lichen Nitidus. Presented by DR C GUY LANE, Boston

The patient, a 24 year old white woman, six months before entrance to the hospital, noticed a tan discoloration of the skin on the flexor surface of the wrists. There were no accompanying symptoms. Soon thereafter similar lesions appeared at the elbows, along the arms near the anterior axillary folds and on the skin over the clavicles. She now presents on the flexor surface of both wrists a circumscribed tan area of dermatitis which on closer examination is shown to be made up of individual small glistening papules. The circumscribed area of involvement on the elbows, neck and arms is the color of normal skin and consists of individual yellow-brown papules with shining tops.

Microscopic examination revealed a picture suggestive of lichen nitidus.

Scleroderma (Progressive Type) Presented by DR J H SWARTZ, Boston

Eight months ago this 28 year old woman noticed stiffness of her fingers, which progressively became worse. Shortly thereafter red macules appeared over the shins and walking became painful. Swelling of the cheeks and eyelids appeared. She noticed that her hands and feet became painful and purple when exposed to cold. The entire process has progressed, making motion difficult.

There is woody edema of the fingers, the dorsa of the hands and wrists, the ankles, the sternocleidomastoid region, the knees, the cheeks, the upper part of the chest and the abdomen. The skin is tense, shiny and thickened, and wrinkles are obliterated. Motion of the fingers, wrists, neck and knees is limited. The hands and feet are cold and cyanotic.

Microscopic examination showed scleroderma.

Under treatment with daily injections of solution of posterior pituitary (double U S P strength) the patient has improved somewhat. A bilateral dorsal sympathectomy has been done.

DISCUSSION

DR WILLIAM P BOARDMAN, Boston. The process does not seem to be generalized at present. It may be that treatment has been effective in a short time. In some cases this condition in children clears up spontaneously. I wonder whether the change that has taken place was spontaneous or was due to the therapy.

DR J H SWARTZ, Boston. I prefer to call this condition progressive rather than generalized scleroderma. The changes have been striking as far as changes in cutaneous temperature and consistency of the skin are concerned. The porklike feeling has disappeared to a considerable extent. I have not seen the patient for a long time since the operation, and she has made a decided improvement since the excision was done.

Discoid Lupus Erythematosus with Dissemination Presented by DR MAURICE MYER TOLMAN, Boston

This 23 year old woman had a condition diagnosed in 1936 as discoid lupus erythematosus. She was admitted to the hospital on April 12, 1938, with cervical adenopathy, fever and recurrence of lesions. The white blood cell counts were 2,950 and 4,150 per cubic millimeter. She was discharged and followed in the outpatient department. She was seen again on Nov 3, 1938, with a flare-up of the old lesions and the appearance of new ones. At that time the white blood cell count was 2,400 per cubic millimeter. She was admitted to the hospital November 25 at which time the white blood cell count was 3,600. Treatment with nicotinic acid was started on November 28. There was a severe vasomotor reaction to 150 mg three times a day. On December 6 the patient had a chill and her temperature rose to 103.4 F. After five days on 500 mg daily the white blood cell count was 2,500. She was given five blood transfusions of 500 cc each and snake venom in a 1 to 3,000 dilution subcutaneously, starting on December 9. Petechiae and bullous lesions developed, and the leukocyte count was as low as 1,900 per cubic millimeter. There was decided improvement after four or five days, and she recovered.

At present there are scattered over her face and neck numerous slightly elevated, reddish macules from 3 to 10 mm in diameter, which do not fade entirely under pressure and are covered with a grayish to yellowish adherent scale. The entire face and neck appear flushed. The lesions below the eyes and over the nose are confluent.

DISCUSSION

DR MAURICE MYER TOLMAN, Boston. This case presents several interesting phases. One is the fact that a patient with disseminated lupus erythematosus will recover only if the primary manifestation of the disease has been chronic discoid lesions, recovery does not occur if the onset is acute. Another is the question of hemorrhage in the final stages of the acute disseminated forms of lupus erythema-

tosus, and the third is the question of what role nicotinic acid may have played in the flare-up of this acute condition. This girl showed symptoms of a downhill course prior to the giving of nicotinic acid, manifested by a general feeling of malaise and loss of strength, and there was also a downward tendency of the white blood cell count. When I saw her that day I considered a flare-up probable and sent her into the ward. It was while she was there that nicotinic acid was given. She showed after the first dose a much greater amount of vasomotor flushing than is usually seen, and after the substance had been given for about five days in rather large doses complete dissemination occurred, she was gravely ill and was practically moribund when administration of snake venom was started. I was interested in starting snake venom treatment because I have been interested for some time in seeing patients with this disease while dying bleed and ooze from the gums and other mucous membranes and at autopsy show in the viscera, especially in the stomach, a pool of unclotted blood. Together with the particular type of hemorrhage that one looks for in the extremities, it occurred to my associates and me that this might be some form of ectasia of the minute vessels of the skin. We performed a snake venom test, which at first elicited no reaction. This is consistent with the fact that the chronic discoid lesions do not show reactions to snake venom, whereas the acute ones do. The second test did elicit a reaction, whether it was a coincidence or not, I do not know. Coincidentally with the giving of snake venom in at first minute and then daily larger doses, the girl turned from a practically moribund patient into one who began to feel better, the hemorrhages quieted down, the white cell count, which had gone as low as 1,900 per cubic millimeter, began to go up, and she has been perfectly well ever since. It is only recently, with a slight phalangeal upset, that she has shown any sign of cutaneous lesions. I do not know whether nicotinic acid played any role in the flare-up.

DR FRANCIS M. THURMON, Boston. I should like to say that I have had 2 patients with acute disseminated lupus erythematosus who were gravely ill, and they were treated with snake venom. It is my feeling that it was the snake venom that saved their lives. Both were young girls. The basis for using snake venom was the presence of the hemorrhagic phase of the acute lupus erythematosus, which was proved by the tourniquet test applied above the elbow.

DR E. WILLIAM ABRAMOWITZ, New York (by invitation). Of course, hemorrhagic purpura has been reported in cases of disseminated lupus erythematosus. I treated a patient who had had his spleen removed. It may be a passing phase of this disease about which not much is known. Physicians in New York have not had any startling results, so far as I know, with snake venom. It has been used for hemorrhagic purpura mainly. I have been following a different procedure. Up to about two years ago I signed about 5 or 6 death certificates every year of patients who died of acute disseminated lupus erythematosus. I have not signed any since. I started to use sulfanilamide, at first in intensive doses, which I had to discontinue on account of the drop in the platelet count. Since then I have used small doses, 5 grains (0.32 Gm.) three or four times a day. I still take blood counts. I have not encountered any reactions, but at times a patient may have general symptoms of gastric distress and I am obliged to discontinue the drug. In that event I give quinine in the interval and after a time return to the sulfanilamide. I have not done this for the discoid type of condition except in isolated cases in which it has been resistant to gold and bismuth therapy, but I have sent 4 patients with acute disseminated lupus erythematosus out of the hospital and have had others for whom the prognosis was very grave and who have recovered—I do not say they are cured, because it is necessary to watch them for a period of years. The results have, however, been spectacular.

DR MAURICE MYER TOLMAN, Boston. As I remember it, this patient was given several transfusions, one prior to the use of snake venom, apparently without any effect on the disease, and one about a day before snake venom treatment was

instituted, and the question was discussed whether the transfusion played any particular part in her recovery. I think it is important to know at which stage of disseminated lupus erythematosus certain forms of therapy are instituted. I think all will agree that the acute type is the manifestation of some toxin probably acting on the blood vessel wall or the minute vessels of the skin. Now if one can attack the toxin before it has done its damage to the vessel wall and if it is streptococcic, sulfanilamide will control it. I think the rationale of snake venom therapy is that the venom counteracts the disease by bolstering up the wall itself. This action is a little different from that observed in treatment of the type of purpura manifested by the tourniquet test, which represents an increase in the pressure of the endothelial system of the wall and the action of nicotinic acid. This is a direct action on the wall by the toxin, if the snake venom has done anything, it has bolstered up the wall itself and has had no effect on the toxin.

FREDERICK S. BURNS, M.D., *President*

BERNARD APPEL, M.D., *Secretary*

Boston, April 12, 1939

Lichenoid Dermatitis? Presented by DR. W. P. BOARDMAN, Boston

Ten weeks ago this man, aged 39, began to have lesions with itching on the scalp, forehead, trunk and extremities. On the advice of his druggist he used a sulfur ointment without benefit. There is no history of internal medication or dietary change. There now appear pinhead-sized round erythematous papules on the abdomen, buttocks and extremities, especially on the extensor surfaces of the extremities.

The patient's white blood cell count was 5,000 per cubic millimeter, and the red blood cell count, 5,000,000 per cubic millimeter, with hemoglobin 81 per cent, and eosinophils 20 per cent.

Treatment has consisted of the administration of calcium gluconate and piodrine hydrochloride, and starch baths, with no benefit. Enesol caused temporary improvement.

DISCUSSION

DR. J. H. BLAISDELL, Boston. Diagnoses other than lichenoid dermatitis seem possible to me. I suggest, for purposes of discussion, dermatitis herpetiformis or a papular type of urticaria.

DR. F. P. MCCARTHY, Boston. On the patient's first visit I made the diagnosis of toxic dermatitis. The question arises whether one is justified in using this term, as it does not appear in many textbooks as designating an entity, although hospital records indicate its wide use.

DR. J. MULLER, Worcester, Mass. The interesting feature in the laboratory report was 20 per cent eosinophils, and I think that this rather supports the diagnosis of a papular type of urticaria. If this diagnosis is right, one must think of sensitivity to certain foods. I think some dietary measures might be tried, possibly with good results. The treatment by medicines has not accomplished much.

DR. F. P. MCCARTHY, Boston. May I inquire in what percentage of cases chronic urticaria is due to food sensitivity, as determined by local cutaneous tests for allergy? My impression is that in cases of chronic urticaria of prolonged duration the percentage of positive reactions is very small. I also question whether a dietary restriction in any way would modify the progress of the case.

DR. P. C. BAIRD, Boston. I can answer that question. Allergists state that the results of the tests are negative in 98 per cent of the cases. In the other 2 per cent the reactions are usually so extensively positive as to make interpreta-

tion difficult In regard to diet, elimination diets have proved to be of considerable service in occasional cases

DR J MULLER, Worcester, Mass May I disagree with the preceding speaker? Elimination diets give much better results than cutaneous tests, but I still do not believe that there is a method in medicine which should give 98 per cent false results I do not claim for the cutaneous tests anywhere near the reliability which some people do, but I do not think that they are wrong 98 times out of 100 I have made a good many tests, and perhaps in one third of my cases I got some information I shall have to add that in several cases in which I did get a positive reaction the response to the dietary regimen which I instituted on the basis of it proved that the reaction, or my interpretation of the reaction, was false I fully agree with Dr Baird that an elimination diet is the way to treat this patient Cutaneous tests could not be performed at present, since there is insufficient healthy skin left

DR E C WEISE, Bridgeport, Conn I think Dr Baird was misunderstood He did not say that 98 per cent of the results of cutaneous tests in patients with this condition were wrong or false He did say, as I understood him, that 98 per cent of the tests gave negative results Another point is that I do not see how one could do scratch or intradermal tests on this particular patient because of the severe dermatographism which he presents One can hardly touch his skin without producing a wheal, so intradermal or scratch tests are really out of the question at present

Lichen Planus Sclerosus et Atrophicus? Dermatitis Lichenoides Chronica Atrophicans (Csillag)? Presented by DR G SCHWARTZ, Boston

This woman, aged 58, was first seen in 1931, at which time she complained of itching in the axillas and around the vulva The lesions were dry and scaly In 1932 lesions appeared under the breasts, and a few months later she complained of general pruritus, but there were no new lesions In 1933 she had a partial vulvectomy for supposed kraurosis vulvae After this she was treated for a generalized papular rash at the Beth Israel Hospital and later at the Massachusetts General Hospital She returned to this clinic one month ago

The patient now shows multiple large diffuse areas arranged symmetrically about the neck, in the axillas, under the breasts, on the abdomen and about the perineum and vagina She claims that there is intense itching on all parts involved The lesions are dry, crepe-paper-like, wrinkled atrophic scars, with little thickening The lesions are sharply outlined and white to silver in color

DISCUSSION

DR G SCHWARTZ, Boston I think that this condition resembles dermatitis lichenoides chronica atrophicans, as described by Ormsby (Ormsby, O S Diseases of the Skin, ed 5, Philadelphia, Lea & Febiger, 1939, p 559) He makes a differential diagnosis between it and lichen planus atrophicus in that there are no black, horny plugs filling in the punctate depressions that one sees first in lichen planus, and he claims that histologically it resembles scleroderma and is believed by many to be an atypical form of scleroderma

Nodular Myxedema in a Case of Thyrotoxicosis Presented by DR J G DOWNING, Boston

On May 10, 1937, this patient, a seaman, reported to the custom house complaining of a dermatitis of the lower thirds of both legs He was referred to the United States Marine Hospital, where he was treated until July 15, for the dermatitis and also for hyperthyroidism, because his basal metabolic rate was +17 per cent on July 12

On July 15 the patient was admitted to the United States Marine Hospital with a diagnosis of hyperthyroidism and scleroderma He was studied from

July 16 until August 3, during which time his basal metabolic rate was found to be +38 per cent. On August 8 he was transferred to the surgical service, and on August 14 a partial thyroidectomy was performed, with removal of practically all the right lobe of the thyroid. The left lobe was not operated on, because of a rise in the pulse rate while he was on the operating table. On September 9 the patient's basal metabolic rate was +4 per cent, and the next day he was transferred to the outpatient department. On November 4 the patient was seen for the first time after discharge to the outpatient department and was found to have a pronounced tremor. He was admitted again on December 13. From Dec 13 to Jan 25, 1938, the patient was studied, and during this time his basal metabolic rate was found to range between +55 per cent, on admission, to +21 per cent, just before he was operated on the second time, on January 25. Half of the remaining portion of the right lobe and seven eighths of the intact left lobe were removed. The convalescence was uncomplicated. On March 2 he was transferred to the outpatient department. The condition of his legs was not much affected by either of these hospitalizations and operations. The patient has been kept under outpatient observation from March 17 to the present time. During the greater part of this period he has been taking iodine in some form, such as compound solution of iodine or hydriodic acid. At present he is maintaining a constant weight of approximately 145 pounds (65.8 Kg) and is not nervous.

Microscopic examination showed a typical picture of localized myxedema of the skin.

DISCUSSION

DR R JACOBY, Boston. I should like to suggest lymphangioma circumscriptum.

DR P BAIRD, Boston. My impression is that more cases of circumscribed myxedema have been reported from Dr Stokes's clinic in Philadelphia than perhaps from most of the other places in the world. I should like to suggest that Dr Anderson, who is a guest of the society today and who was associated with Dr Stokes for five years, be invited to make a few remarks in reference to this case.

DR L E ANDERSON, Springfield, Mass. I agree with the diagnosis of circumscribed myxedema in this patient. It is true that Dr Pillsbury from Stokes's clinic did report a fairly large series of patients with this condition. I personally saw only 2 or 3 of them. The condition of the patients whom I saw was similar to this. The pigskin appearance in this patient, I think, is typical. Circumscribed lymphangioma, I think, can be ruled out definitely. This patient has had none of the semisolid vesicles that are usually in a picture of lymphangioma circumscriptum, and no scarring from former pseudovesicular lesions. The patient certainly appears to be the type in whom one would expect to observe a circumscribed myxedema, because he still has some of the outward signs of hyperthyroidism. He still has some xanthoma. The circumscribed myxedema occurs paradoxically in patients with a basal metabolic rate above normal. In other words, the condition is a localized myxedema in a generalized hyperthyroidism.

DR E M STANDISH, Hartford, Conn. I think Dr Anderson explains the situation clearly, because in this particular case the myxedema occurred before the thyroidectomy was performed. If I recall correctly, in Cleveland at the meeting of the American Medical Association four or five years ago, there were 4 or 5 cases in which unilateral myxedema occurred after complete thyroidectomy, and at the time the warning was brought out that a total thyroidectomy should never be performed. Is that so, Dr Anderson? Does the condition in some cases occur after thyroidectomy or, as in this one, does it always occur before?

DR L E ANDERSON, Springfield, Mass. I think that in some of the cases the condition occurred after thyroidectomy, but in such cases the thyroidectomy was not complete, and the patient had a recurrence.

DR J G DOWNING, Boston I think that the largest number of cases was reported by Dr Paul O'Leary The case presented is interesting because the condition appeared before there were any operative procedures There may be 1 or 2 such cases in the literature, in the majority the condition occurs after either partial or complete thyroidectomy This patient did have some of the translucent vesicles which are described in circumscribed lymphangioma These were seen to be solid masses of mucin on histologic examination The interesting and unusual lesions on both legs showed brilliant red areas in the center and a bluish red discoloration at the periphery At the present time the color has disappeared There has been definite improvement in both legs It was noteworthy that this man suffered from intolerable itching and that after the thyroidectomy the itching disappeared

DR F P MCCARTHY, Boston The patient states that the condition came on overnight and within a very short time reached the size it now presents The condition began in the winter, and there is a question of frostbite as the activating factor, which would tend to localize the lesion The pathologic picture is that of a true mucous edema of the skin, and the sudden onset is extremely interesting, provided the history is correct

Granuloma Annulare Presented by DR E A LAFRANIERE, Arlington, Mass

Several months ago a lesion appeared on the left leg of this Negro child, aged 4 years, and has not changed in appearance since then The lesion is circular, consisting of a ring about 2 cm in diameter and nodules about 2 mm in diameter, on the left leg near the knee

Physical examination showed coarse rhonchi in the chest Stereoscopic examination of the chest showed thickening of the right hilus, with areas of peribronchial infiltration extending down from it into the base of the right lung There is a questionable area of beginning calcification, about $\frac{3}{4}$ inch (0.6 cm) in diameter, in the right hilus

There is a question of childhood tuberculosis and bronchitis No evidence of pulmonary tuberculosis was found

DISCUSSION

DR F A CHACE, Fall River, Mass I agree with the diagnosis

Lichen Planus Atrophicus? Morphea? Presented by DR C GUY LANE, Boston

For the past six years this woman, aged 20, has noticed the occasional appearance of small pale spots on the upper part of her back, some of which have slowly enlarged, producing what appears to her to be white scars Scattered across the upper part of the back are a number of macular and maculopapular lesions varying in color from pale white in the smaller to ivory in the larger ones The larger patches are slightly raised and present a definite thin red border Some of the larger patches are kidney shaped The skin overlying these lesions is atrophic

DISCUSSION

DR B APPEL, Boston I think that the picture presented by this patient is perhaps a little bit more typical of lichen planus atrophicus than is that in the case presented by Dr Schwartz, although I am not prepared to differentiate between the two diagnoses proposed for the previous condition In this particular instance, the lesions are fairly characteristic, showing closely placed follicular plugging, with silvery white, dry, atrophic, sharply outlined areas In my opinion this case is a fairly classic one of lichen planus atrophicus

Pseudo Xanthoma Elasticum? Presented by DR C GUY LANE, Boston

About ten years ago this man, aged 26, noticed that the skin on the left side of his neck was becoming a mottled yellow This process slowly extended around to the right side of the neck There have been no subjective symptoms The

patient states that the cervical lymph glands on the left were enlarged previous to the appearance of the neck lesions. The papules do not become pigmented in summer.

Involving most of the left side of the neck and extending around to the right are groups of small shiny yellowish to pink firm papules. Individual lesions measure 1 to 1.5 mm in diameter and are often grouped in an irregular linear arrangement, averaging 1.5 cm. In places the lesions have coalesced.

DISCUSSION

DR M. M. TOLMAN, Chelsea, Mass. I should like to ask if anybody examined this man's eyegrounds. I noticed no mention of it on the record.

DR C. GUY LANE, Boston. He was examined recently, but I do not know whether there has been any examination of the eyegrounds or not.

DR J. G. DOWNING, Boston. I suggest the diagnosis lymphangioma circumscriptum.

DR E. C. WEISE, Bridgeport, Conn. I agree with the diagnosis as presented, pseudo xanthoma elasticum. The clinical appearance is typical. As to the eyeground findings, I procured an ophthalmoscope and examined the eyegrounds under difficulties. I could not see any angioid streaks, however, that does not mean that they are not there. It would be a good plan to have an ophthalmologist check the fundi.

Erythema Multiforme. Presented by DR W. P. BOARDMAN, Boston

About two months ago this woman, aged 28, was bedridden with grip and was taking many pills prescribed by her doctor. She recovered from this, and a pain developed in her chest, which lasted for a week. About one month ago her present eruption developed. She continued taking the pills till about three weeks ago.

She now presents erythematous papules over the dorsa of both elbows, mixed macular purpuric lesions and larger purpuric areas on the buttocks, thighs and legs. There are also many hemorrhagic bullae and vesicles present. There are also several ulcerated lesions.

DISCUSSION

DR J. H. BLAISDELL, Boston. I should like to inquire if it is possible for a patient to have erythema multiforme for a month with an extensive eruption but without any malaise or recurrent attacks, and also to have it limited to the legs, with none on the backs of the hands, the lower parts of the arms or the mouth.

DR B. APPEL, Boston. When this patient was seen in the clinic, she had fairly active lesions on the extensor surface of the arms near the elbows, but they have largely subsided. She had no lesions in the mouth.

DR E. C. WEISE, Bridgeport, Conn. I should like to make the suggestion that this so-called grip which the patient is stated to have had was no more than the prodromal symptoms or the constitutional symptoms of the impending erythema multiforme. One often finds this in the history, the patient has a little malaise, feels a little "grippy," complains of a sort throat and a short time later has the erythema multiforme eruption. I thought that I saw the remains of old lesions on the extensor surface of the arms near the elbows, and of course active lesions are still present on the buttocks and legs.

Lupus Erythematosus? Presented by DR M. M. TOLMAN, Chelsea, Mass

This woman, aged 21, six months ago first noticed on her left cheek one or two small red spots, which developed into "blisters" and increased in size. Gradually new lesions appeared on the right cheek. The appearance and the spread of this condition have always been associated with the presence of vesicles. The condition is asymptomatic except for an occasional mild burning or drying sensation.

Scattered over her face, but generally confined to the medial portions of the cheeks, are eight red round to oval macules, varying from 1 to 4 cm in diameter. Central paling is present in some, and a questionable atrophy seems to be present in all. At the time of examination all the lesions presented definite small vesicles at the periphery. In some of the lesions an occasional vesicle could be found within the border. There are no lesions in the mouth. Otherwise the results of physical examination are essentially normal.

Cultures from vesicles show *Staphylococcus aureus*.

Treatment has consisted of weekly intramuscular injections of 2 cc of bismuth subsalicylate, but the lesions are progressing.

DISCUSSION

DR M M TOLMAN, Chelsea, Mass. There was a suggestion that the patient might have leprosy. Nasal smears and stains were made, but Hansen bacilli were not found.

Tertiary Syphilodermas Presented by DR W P BOARDMAN, Boston

This woman, aged 46, states that about five years ago she had "a few injections" for syphilis. About two years ago she had an eruption which disappeared after a few weeks. Her present eruption began about three and one-half months ago, and new lesions have been appearing continuously. There is some itching.

The eruption is symmetric and consists of nodular dull red grouped lesions, circularly arranged on the face, arms, hands and trunk, with a few lesions on the legs. There is no scarring, and there is slight scaling.

A Hinton test of the blood gave a positive result.

She had one injection of a bismuth preparation one week ago.

DISCUSSION

DR A W CHEEVER, Boston. It is difficult for me to understand the diagnosis of tertiary syphilis. It seems to me that the condition should be classed as a recurring type of secondary syphilis, of which I think it is a reasonably typical example of a rather rare type, the corymbiform. I have observed corymbiform lesions more on the back, it seems to me, than where she has them. I understand that the patient had had just a small amount of treatment, five or six injections, and then had quit. It seems to me that the insufficient treatment would increase the tendency to recurrence.

Lupus Vulgaris? Syphilis? Presented by DR F RONCHESI, Providence, R I

This man, aged 56, has an annular nodular lesion on the right gluteal region, which has been present about three years. He has had diabetes since 1936.

Microscopic examination showed vegetative dermatitis.

DISCUSSION

DR J H BLAISDELL, Boston. I favor the diagnosis of syphilis for the following reasons. This man presents a chronic destructive condition, and when such a condition is present one should always think of syphilis, tuberculosis and cancer. Obviously the condition is not cancer in this case. Against the diagnosis of lupus vulgaris is the man's age, 56, also the three year duration is a reasonably short time for lupus vulgaris to produce a lesion of this size. The scarring is superficial, and there is little recurrence. There is an area several inches in diameter with only one or two nodules. On the other hand, the condition would seem to be consistent with a diagnosis of a later syphilitic lesion, in spite of the fact, as I recall it, that several tests of the blood gave negative results.

DR F P MCCARTHY, Boston. The histologic section in this case shows the picture of one of the infectious granulomas.

There is an epithelioid cellular reaction in the presence of a few giant cells but no true miliary tubercle formation, and a definite diagnosis differentiating syphilis from tuberculosis cannot be made from the slide

I favor the diagnosis of syphilis, based particularly on the clinical picture

Lupus Vulgaris Presented by DR B APPEL, Boston

Eighteen years ago in this man, aged 43, an eruption developed on the right side of the face several months after there had been a burn in that location. There was a progression of lesions to the left cheek and nose three years ago, and there has been secondary infection for the past few months while he has not had therapy.

At present there are erythematous, scaly, nodular, crusted lesions of butterfly-like appearance on the cheeks, nose, right ear and right upper eyelid. The right side of the face is more extensively involved. The lesions are sharply outlined, and there is a tendency to clearing in the center. Scarring is superficial and not deforming. There are typical apple jelly nodules, particularly on the active borders of the lesions. There is also a bismuth line on both gums.

Microscopic examination in 1935 showed lupus vulgaris.

The patient was treated with ultraviolet rays in 1930, with slight improvement, he had eight injections of a bismuth preparation in 1935, twenty-one injections of gold and sodium thiosulfate in 1935 and in 1936, four injections in 1938, and three injections in 1939.

Lupus Vulgaris (Tumidus) Presented by DR F RONCHESI, Providence, R I

About seven years ago lesions appeared on the forehead, the right postauricular region and the right popliteal space of this man, aged 24. He lost his right arm in a fireworks accident at the age of 5 years. In June 1937, in an automobile accident, he received a laceration requiring several stitches at about the site of the frontal lesion. The clinical appearance of the lesions was suggestive of naevus comedonicus. Microscopic examination showed lupus vulgaris. Inoculation of guinea pigs with tissue gave a positive reaction for tubercle bacilli.

In 1935 the lesion was desiccated and curetted, with a resulting soft scar, which was visible in the center of the lesion.

He has at the present time a soft, elevated, annular, yellowish red lesion on the frontal and temporal region on the right side, with a scar in the center. On the surface are large openings filled with keratotic plugs. No apple jelly nodules are visible under pressure. Similar lesions are present on the right postauricular and on the right popliteal region.

The reaction to a tuberculin test with a dilution of 1:1,000 was positive. Microscopic examination showed lupus vulgaris.

The desiccation and curettage in 1935 were followed with good results. In February and March of 1939 the patient had roentgen ray therapy, with the result that there was some flattening of the treated areas.

DISCUSSION

DR B APPEL, Boston. I should like to suggest that the patient be treated with injections of chaulmoogra oil esters directly into the lesions themselves.

DR J. G. DOWNING, Boston. I have never seen tuberculosis of the skin that looked like this condition, but I have seen similar conditions due to syphilis. Despite the biopsy and report, I still think that this is syphilis of the skin, and I suggest neoarsphenamine and bismuth for treatment.

DR J. H. BLAISDELL, Boston. I should think that the recently described treatment, the injection of starch, U S P, might well be tried here.

DR F. P. MCCARTHY, Boston. The pathologic picture in this case is interesting, as the growth is composed of a diffuse epithelioid tissue, with a few giant cells just under the overlying atrophic epidermis. The picture definitely suggests the usual change seen in lupus vulgaris, and since the injections in guinea pigs produced positive results, the diagnosis of lupus vulgaris must be accepted.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

MERLIN TREVOR-ROPER MAYNARD, M D, *President*.H V ALLINGTON, M D, *Secretary**April 21, 1939***Pseudopelade** Presented by DR ERVIN EPSTEIN, Oakland, Calif

R M, a white woman aged 32, was referred to me by Dr Joseph Reis on March 16, 1939. She stated that she had suffered from "eczema" of the scalp for the past twelve years. A small bald spot had appeared on the top of her scalp at the onset. This had not changed particularly until about one year ago, when it started to enlarge.

She now has an irregular palm-sized area of alopecia with atrophy of the scalp. Inflammatory changes are not noted. A few hairs remain in this area, but they can be easily and painlessly extracted. The entire scalp is involved in a dry, scaling eruption which in places is ichthyosiform. There is no history of pustulation. Except for a mild postauricular intertriginous dermatitis there are no lesions of the skin or mucous membranes. The nails are not involved.

Microscopic examination of the hair in warmed 15 per cent solution of potassium hydroxide and culture on Sabouraud's mediums failed to reveal any fungi. Wassermann and Kahn tests of the blood gave negative results.

Therapy to date has consisted of local application of 5 per cent ammoniated mercury ointment plus one subfractional dose of unfiltered roentgen rays.

DISCUSSION

DR G V KULCHAR I suggest a trial of iontophoresis with acetyl-beta-methylcholine.

DR A E INGELS I have seen eruptions that appeared at first to be folliculitis decalvans but later showed features common to pseudopelade. I should like to hear some opinion as to whether one should attempt to differentiate these two conditions or whether they are the same.

DR HIRAM E MILLER I have given up attempting to classify these conditions except to call them cicatrizing alopecia of the scalp. When lupus erythematosus is definitely ruled out, I do not feel that it is possible, or perhaps even therapeutically useful, to classify them further.

DR J D VIECELLI It is sometimes difficult in a case of cicatrizing alopecia of the scalp to rule out lupus erythematosus.

Tryparsamide Dermatitis Presented by DR ERVIN EPSTEIN, Oakland, Calif

W L, a white man aged 62, has received eighty-five injections of bismuth subsalicylate, 57 of tryparsamide (each 3 Gm) and ten fever treatments for tabes dorsalis.

On Feb 15, 1939 he received the fifth injection in a course of tryparsamide therapy and the same evening he noted pruritus of the dorsa of both hands, the calves, the scalp and the back of the neck. An ill defined eruption appeared in these areas. He was given another intravenous dose of tryparsamide on March 1, which resulted in more severe itching and a more definite eruption. This improved but had not completely subsided when he was given another injection of tryparsamide, one week later. The pruritus and the eruption became more severe.

When first seen by me, on March 10, he presented an erythematous, vesicular, weeping and crusted eruption involving the backs of the hands. On the legs the eruption consisted of an indefinite pruritic area with small erythematous

papules sparsely covering both calves. A number of excoriations were present on the scalp. The back of the neck was involved in an eczematoid eruption with a few excoriated papules.

Tryparsamide was discontinued, and the eruption cleared in about two weeks. On April 14, 3 Gm of tryparsamide was injected intravenously, with prompt recurrence of the dermatitis. A similar injection was administered on April 19, causing a further exacerbation.

DISCUSSION

DR H J TEMPLETON, Oakland, Calif. The patient stated to me that soap irritates his hands very badly. I suggest that Dr Epstein try having him rinse his hands in a 1 per cent solution of sodium hexametaphosphate. This substance is said to act as a buffer and to reduce the pH of soapy water, the calcium and magnesium ions are immobilized by it so that they are unable to form irritating insoluble soaps.

DR C J LUNSFORD, Oakland, Calif. What are the theoretic limitations of the amount of tryparsamide which may safely be given to patients with syphilis of the central nervous system? I have a patient to whom I have given about one hundred and fifty injections of tryparsamide without any reaction and I remember reading some case reports by Dr Solomon of Boston who gave patients as much as two hundred to three hundred injections without untoward results.

DR G V KULCHAR. It is not clear to me whether the lesion in the present case appeared in the same place every time.

DR MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif. The patient stated that he had a good deal of gaseous distention after every injection. This made me wonder whether the eruption is of gastrointestinal origin and is precipitated by sensitivity to sunlight.

DR N N EPSTEIN. Tryparsamide is tolerated well as a rule, in many cases for long courses of injections. I have recently seen 2 patients who had a serious type of acute reaction. In 1 patient this was fatal. The only tryparsamide eruptions I have seen have followed arsphenamine dermatitis.

DR ERVIN EPSTEIN, Oakland, Calif. This patient's eruption recurred in the same location each time, which classes it as a fixed eruption. Cutaneous complications following tryparsamide therapy are rare. According to the cooperative clinical studies, tryparsamide is the least cutaneotoxic of any of the arsphenamines studied (Cole, H N, and others. Cooperative Clinical Studies in the Treatment of Syphilis, Arsenical Reactions, *Ven Dis Inform* 14:173 [Aug] 1933). About the relation of tryparsamide dermatitis to past sensitivity to trivalent arsenicals, 6 of 31 patients showing sensitivity of the skin to the arsphenamines were proved by patch tests to be sensitive to tryparsamide also (Epstein, E. Sensitivity to Both Trivalent and Pentavalent Arsenicals, *ARCH DERMAT & SYPH* 36:964 [Nov] 1937). Also, I have observed a case of an exfoliative dermatitis and death due to carbarsone, which is chemically closely related to tryparsamide (Epstein, E. Toxicity of Carbarsone, *J A M A* 106:769 [March 7] 1936).

Pemphigus of the Conjunctiva. Presented by DR HIRAM E MILLER

D N, a white American aged 66, entered the dermatologic clinic on April 18, 1939. His complaints were of a sore mouth and reddened and painful eyes.

A clinical record of two years ago describes pyorrhea accompanied by small white blisters on the oral mucous membrane and thickened eyelids with marked reddening and definite scarring of the conjunctivas.

Recent examination of the mouth disclosed bullous lesions varying from 5 to 20 mm in diameter, surrounded by a circumscribed red border. These lesions were scattered along the gingival margins and the buccal mucosa and extended into the laryngeal portion of the pharynx, the epiglottis and the soft tissues were involved. The nose was free of lesions. The eyelids were injected and scarred,

and small vesicles were seen near the limbus of the right eye. There were no cutaneous manifestations except one bullous lesion on the penis, near the sulcus. The observations at physical examination were otherwise noncontributory.

DISCUSSION

DR H J TEMPLETON, Oakland, Calif. We are privileged in being able to observe this case of ocular pemphigus because of the rarity of the condition. It is called "essential shrinkage of the conjunctiva" by the ophthalmologists.

DR HIRAM E MILLER. I was somewhat surprised to see a positive diagnosis of pemphigus at the head of this case history. It was a tentative diagnosis only. Dr Templeton's reference to essential shrinkage of the conjunctiva is of interest. This patient had been in the clinic for patients with ocular diseases two years previously, and that was the actual diagnosis made at that time.

Pseudoatrophoderma Colli(?) Presented by DR C E SCHOFF, Sacramento, Calif

J S P, a white housewife aged 50, has had an eruption on her neck for eighteen or nineteen years. It began symmetrically on the anterolateral surface of the neck without apparent cause and has spread slowly.

At present the involved area shows a retiform pigmentary change which includes the lateral and the anterior surface of the neck to a point 1 inch (2.5 cm) below the suprasternal notch. On close inspection it is noted that there are areas varying from 0.2 to 0.5 cm in diameter which are depigmented and apparently lighter than the normal surrounding (brunette) skin. These areas have the appearance of being atrophic. Surrounding these are hyperpigmented folds of skin. There are no subjective symptoms associated with this change, nor have there ever been. As a girl the patient used to work in the fields. She has spent most of her life in the Sacramento Valley and the San Francisco Bay region.

She has four children alive and well. One child died at the age of 3 months from intestinal trouble. One daughter, also presented tonight, has a similar pigmentary disturbance. No history of involvement of other members of the family could be obtained. A laparotomy was performed three years ago for "tumors of the womb." Since that time the patient has not menstruated.

No change has been noted in the skin which could be attributed to the operation. There has never been any apparent relation between the cutaneous changes and the menstrual cycle.

Kolmer, Kline and Kahn tests gave negative results.

A blood count was normal.

Urinalysis showed a faint trace of albumin, and 8 to 10 finely granular casts, 5 to 7 leukocytes and 2 to 3 erythrocytes per high power dry field.

Pseudoatrophoderma Colli(?) Presented by DR C E SCHOFF, Sacramento, Calif

D S, a white woman aged 30, a daughter of the patient just presented, demonstrates a similar anomaly of pigmentation, affecting the anterior lateral surfaces of the neck and the upper anterior part of the chest. This began insidiously in the suprasternal notch three or four years ago.

The changes in the skin occupy the areas of the base of the neck and the exposed surfaces of the upper part of the chest. The skin appears folded in very fine cross rugae. These folds show an increased brownish pigmentation, and the intervals between them appear depigmented, shiny and atrophic. The skin is flexible, and the folds flatten on stretching.

This is the same general picture as is presented by the mother, but it is less marked in all respects except the atrophy. There are no subjective symptoms. There have been no serious illnesses. There was questionable pulmonary tuberculosis at about the twelfth or thirteenth year. At that time there was also a

cessation of the menses for four months, and she was told it was due to the condition of her lungs. She recovered rapidly and has had no further clinical signs of pulmonary involvement.

Kolmer, Kline and Kahn tests gave negative results. The blood count and the urine were normal.

DISCUSSION OF CASES OF PSEUDOATROPHODERMA COLLI

DR A E INGELS. In the differential diagnosis it might be well to think of *acanthosis nigricans*.

DR H J TEMPLETON, Oakland, Calif. I wish to differ from the diagnosis, basing my opinion on my experience with 1 patient. Some time ago, shortly after Becker published his description, I presented before this society a patient with a condition that I labeled *pseudoatrophoderma colli*. Recently Dr Becker saw her with me and agreed with the diagnosis. However, her condition does not look anything like that of this patient. Her lesions are depigmented and flat and vary from a few millimeters to 1 cm in diameter. They have a sheen and a crinkly appearance.

DR ERVIN EPSTEIN, Oakland, Calif. The patients studied by Becker and Muir (Becker, S W, and Muir, K B. *Pseudoatrophoderma Colli*, *ARCH DERMAT & SYPH* 29:55 [Jan] 1934) and by Frost and me (paper to be read at the 1939 meeting of the American Dermatological Association) were young women. The lesions apparently clear spontaneously at some time. No cases have been reported in which the patients were elderly persons. After bathing the lesions are usually clearer because the parakeratotic scale is removed. It is this scale rather than true pigmentation that causes the color. The lesions tend to follow the lines of cleavage of the skin. As they clear, they leave a whitish area which resembles atrophic skin. The darkened skin is thrown up into tiny folds.

DR J M GRAVES. I think it would be wise to perform a biopsy and look for elastic tissue. I think it is possible that this is *pseudoxanthoma elasticum*.

DR H V ALLINGTON, Oakland, Calif. I was likewise about to suggest the diagnosis of *pseudoxanthoma elasticum*.

DR HIRAM E MILLER. From this one examination, I am inclined to agree with the diagnosis of *pseudoatrophoderma colli*. There is a rather diffuse hyperpigmentation with some depigmentation, and the epidermis is thrown up into folds. The diagnosis of *pseudoxanthoma elasticum* must be considered. The yellowish, discrete, pinhead-sized to pea-sized papules seen in that disease are not present in this patient, however. *Pseudoxanthoma elasticum* does have a tendency to occur in more than one member of a family, as is observed in these 2 patients. As far as I know, a familial tendency of *pseudoatrophoderma colli* has not been reported. Examination of the eyegrounds to determine the presence or absence of angioid streaks would be of value.

Arsenical Pigmentation and Keratoses. Presented by DR HIRAM E MILLER

A J, an American-born Chinese man aged 22, entered the University of California medical clinic complaining of periodic attacks of asthma since the age of 5 years. He has had no previous medical consultation and has relied on Chinese herbs and pills for relief. During the past two years he has noticed that his skin was becoming darker and that calluses were developing on his palms and soles.

There is diffuse pigmentation of the skin, most pronounced on the trunk. This pigmentation is mottled and grayish. The skin is dry and warm, but there is no scaling. There are numerous punctate hyperkeratotic areas on the palms and soles.

Physical examination otherwise gives essentially negative results. Roentgenograms of the chest were normal. Roentgenograms of the paranasal sinuses showed slight cloudiness of the antrums and the ethmoid cells.

Chemical analysis of the urine did not reveal arsenic. Chemical analysis of the hair has not yet been reported on.

DISCUSSION

DR FRANCES TORRILY: I felt that if this were a case of arsenical pigmentation one ought to be able to find some evidence of arsenic in the urine or in the hair. Up to the present time this has not been found. If the patient had continued to ingest arsenic in pills over a long period until recently, there should be some laboratory evidence of it.

DR H. J. TEMPLETON, Oakland, Calif.: This is as classic a picture of arsenical pigmentation and keratoses as one could find. If this is not arsenical dermatitis, the whole idea of the picture must be revised.

DR G. V. KULCHAR: Why not give a test dose of sodium thiosulfate?

DR MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif.: Is it not true that when patients are no longer taking arsenic, the arsenic cannot be demonstrated in the urine except when sodium thiosulfate is given? I noted that this patient does not have greenish hair.

DR ERNEST K. STRATTON: I suggest microchemical analysis of a biopsy specimen of this patient's skin. The department of pharmacology of the University of California is equipped with apparatus and reagents which show the characteristic crystal formation if arsenic is present.

DR ERVIN EPSTEIN, Oakland, Calif.: One might stain for arsenic in the tissues by the method of Osborne (Osborne, E. D. *Microchemical Studies of Arsenic in Arsenical Dermatitis*, *ARCH. DERMAT. & SYPH.* 18:37 [July] 1928).

DR HIRSH E. MILLER: This is a classic picture of arsenical pigmentation and keratoses. If chemical tests fail to reveal the presence of arsenic, there is something wrong with the tests.

Hydroa Aestivale Presented by DR H. J. TEMPLETON, Oakland, Calif.

F. R. H., a white man aged 43, states that during the last two summers he has noticed pruritic papules wherever the sun strikes his skin. The eruption appears in the spring, persists throughout the summer and disappears during the fall. It is limited to the face, ears, neck and hands. He states that it appears on his trunk if he takes a sun bath. His brother is said to have the same disease. There is no history of reddened urine.

Morphologically the lesions are fairly superficial but perceptibly indurated papules measuring 2 to 5 mm in diameter. A few are capped with vesicles, and some are crusted.

No laboratory work has been done yet.

The patient was instructed to protect one hand with a 4 per cent menthyl salicylate lotion and then to expose both to sunlight experimentally.

DISCUSSION

DR N. N. EPSTEIN: I agree with the suggestion that this is an actinic dermatitis but lacks some of the characteristics of hydroa.

DR H. J. TEMPLETON, Oakland, Calif.: This patient does not show the degree of activity in the lesions that was shown a week ago, probably because he has improved during the recent foggy weather. It seems to me that from a truly scientific standpoint one should refer to his condition as "light sensitivity," to describe the disease from the standpoint of etiology. On the other hand, I do not think one should abandon the old morphologic classification. These lesions are firm, shotty papules, so I think the old term "hydroa aestivale" is a good one.

Atrophic Process of Glans Penis with Epithelioma Presented by DR H. J. TEMPLETON, Oakland, Calif.

R. W. G., a white man aged 54, consulted me on Jan. 16, 1939, because of a dime-sized ulceration of the glans penis which had been present for one and a

half years. There was no regional adenopathy. A biopsy showed grade 3 squamous cell epithelioma. The lesion was radically destroyed by electrodesiccation, and healing occurred in three months.

The mucous membrane of the glans penis, aside from the scarred area, shows a peculiar mottling of whitened and reddened areas. The patient stated that the aforementioned epithelioma began in a similar mottled and reddened area.

Although the diagnoses of leukoplakia, lichen planus and erythroplasia of Queyrat were considered, I feel that the condition belonged more in the group of atrophies, such as balanitis xerotica (analogous to kraurosis vulvae in the female).

DISCUSSION

DR G V KULCHAR. I agree with the diagnosis of balanitis xerotica obliterans.

DR N N EPSTEIN. I agree with that diagnosis.

DR HIRAM E MILLER. It has been our experience in cooperation with the genitourinary staff that local removal of an epithelioma of the glans does not cure the condition. It generally is wise to remove most or all of the organ.

DR J M GRAVES. Don't you think another epithelioma is developing now? There is one crusted lesion.

DR MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif. I do not think one can rule out atrophic lichen planus without a biopsy.

DR H J TEMPLETON, Oakland, Calif. This man is young and virile. He objected to our removing any more of the penis than was necessary.

Syringomyelia (Lumbosacral Type). Presented by DR JOHN M GRAVES

M H, a white American woman aged 23, presents a deformity of the left foot, diminished cutaneous sensation of the left leg and difficulty in walking. On March 13, 1939, there were widening and distortion of the left toes, absence of the fourth toe and absence of all nails. There were bluish discoloration of the skin and a brawny induration of the subcutaneous tissue of the leg and foot. Diminution to absence of pain and temperature sensation was demonstrated to the level of the hip joint. The peroneal group of muscles were atrophic. Neither ankle nor knee jerks were elicited.

The present condition began at the age of 8 as painless ulcerations of the four toes. These healed within a year, but the sense of touch was diminished in the foot. There have been repeated exacerbations of the ulcers, increasing deformity of the foot, progressive difficulty in walking and spreading of the anesthesia.

Sections of a biopsy specimen taken Aug 1, 1930, showed atrophic changes, there was no evidence of leprosy.

DISCUSSION

DR HIRAM E MILLER. We considered the diagnosis of leprosy or syringomyelia in this case. Since a positive diagnosis of leprosy could not be made, we concluded, more by elimination than anything else, that the condition is syringomyelia.

Malignant Melanoma. Presented by DR NORMAN N EPSTEIN

J B, a white man aged 61, first noticed a small nodule on the vertex of the scalp about three months ago. This has increased in size. Examination revealed a bean-sized bluish black nodule in the scalp, surrounded uniformly for a distance of about 1.5 cm by a deposit of coal black pigment.

A small lymph node located posteriorly on the right side of the neck showed metastatic malignant melanoma on pathologic examination. There was no evidence of metastasis elsewhere.

Röntgen ray treatment has been given.

DISCUSSION

DR G V KULCHAR How about application of roentgen rays to the pituitary gland?

DR L R TAUSSIG I was interested in the fact that the radiologists are now willing to treat melanomas. For years they did not want to do so. Recently some of them have become enthusiastic about giving cauterizing doses of roentgen rays for melanoma.

DR H V ALLINGTON, Oakland, Calif Did the patient have any lesion there previously?

DR N N EPSTEIN No, there was no history of any.

A Case for Diagnosis (Pemphigus? Epidermolysis Bullosa?) Presented by DR N N EPSTEIN

M McM, a white man aged 55, had bullae on the hands, scalp and face first in 1936. These became secondarily infected, and persistent pyoderma developed. The patient was never free of lesions, although the condition varied in severity. At one time bullae appeared on the forearms and lower limbs. Many of the lesions have been associated with trauma.

The patient has been a morphine addict and chronically alcoholic.

Various treatments, including injections of coagulen and sulfanilamide, have been given.

Routine laboratory work revealed nothing contributory.

DISCUSSION

DR CHARLES ALBERT SHUMATE This patient was first seen by me several years ago. He had at that time what I believed to be impetiginized lesions. Later bullae developed on his body and in his mouth. The impression at that time was that he had pemphigus. Last fall he claimed that trauma preceded the appearance of each lesion. A diagnosis of epidermolysis bullosa was then considered.

DR N N EPSTEIN This man has had an interesting history. At one time, about a year ago, he had clear bullae which developed without relation to trauma. The condition was thought to be pemphigus. I think, however, that that diagnosis is open to question, because now some trauma appears to be necessary for the appearance of the lesions.

Epidermolysis Bullosa Congenita Presented by DR H J TEMPLETON, Oakland, Calif

B, a white girl aged 3 days, was referred to us by the physician who delivered her, Dr F L Herrick, of Livermore, Calif, because of stripping off of the skin of the hands, feet, lips and trunk.

Dr Herrick stated that when he cleansed the infant's mouth at birth the skin around the lips peeled off. Later it was noted that the skin peeled off of the hands, feet, buttocks and trunk at sites of trauma.

A paternal uncle died at birth of a similar disease which was diagnosed as pemphigus neonatorum. Both parents recently had negative Wassermann reactions.

The diagnosis of bullous syphiloderm was considered but was ruled out on the basis of negative Wassermann reactions of the parents and negative results from dark field examinations of the baby.

Bullous impetigo neonatorum was ruled out because of the existence of the lesions at birth and because of negative smears and cultures of fluid from unruptured blebs.

The diagnoses of epidermolysis bullosa and pemphigus neonatorum have been suggested.

The baby is being treated by tanning the eroded areas with Burwick's dye (brilliant green 1 per cent and crystal violet 1 per cent in 50 per cent alcohol).

She is tube fed, and generous amounts of vitamins are given. Feedings are well tolerated. Although her general strength is better and the older lesions are improving, new areas of skin are still stripping off. The child is now 17 days old.

DISCUSSION

DR ERVIN EPSTEIN, Oakland, Calif. I suggest the use of moccasin snake venom in this case. I used it in 1 case of epidermolysis bullosa. Afterward the bullae were much more difficult to elicit. One can use it in the form of a 1:3,000 solution, starting out with 0.1 cc hypodermically and building up the dose according to the patients' tolerance.

DR MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif. I have followed a family in which the mother, a daughter and a son all had severe epidermolysis bullosa. Anterior pituitary extract was given until both the girl and the boy had hypertrophy of the breasts. No benefit was received.

DR ERNEST K. STRATTON. I should like to have Dr. Templeton try rabies vaccine in this case. In view of the work done by Grace in isolating a virus from subjects with pemphigus, it is not unlikely that a virus is responsible for epidermolysis bullosa also. Experimenters have found that rabbits infected with the virus of rabies cannot be inoculated with the virus of pemphigus and vice versa.

Argyria. Presented by DR N N EPSTEIN.

J B, a white man aged 65, was first seen because of an ashen gray color of the skin of the face, neck and upper portion of the trunk in October 1938. The scleras also were involved.

The patient states that he has used neo-silvol nose drops daily for several years.

On microscopic study, sections from a biopsy specimen taken from the neck on October 19 appeared normal except for a few subepidermoid perivascular collections of lymphocytes, mononuclear phagocytes and a few eosinophils. In some of these areas the phagocytes contained finely divided black pigment. A few of the vessels were engorged. The pigment largely disappeared after treatment with iodine followed by sodium thiosulfate.

DISCUSSION

DR G V KULCHAR. I saw this man after he had used the neo-silvol nose drops only four or five months. He had generalized argyria at that time.

DR A E INGELS. The sections examined with the dark field microscope according to the method described by Eric Hoffmann are striking. Sections stained with Giemsa's stain show the silver deposited densely in a "line" parallel to the basal layer and outlining the hair follicles and the acini of the sweat glands. I examined sections from this man some time ago, when he was a patient at the Laguna Honda Home.

DR N N EPSTEIN. It is interesting in this case that the argyria is most marked on the upper part of the body, close to where the silver was applied.

A Case for Diagnosis (Tuberculous Granuloma of the Nose?). Presented by DR FRANCES TORREY.

J B, an American boy aged 13, entered the University of California dermatologic clinic complaining of swelling of the nose and difficulty in breathing for the past month.

Excision of tuberculous cervical glands had been done at the age of 1 year and again at the age of 2 years. At the age of 5 years the patient had tuberculosis of the thoracic portion of the spine and was treated at the Shriner's Hospital. At the age of 8 years he had lacrimation of the right eye with a subsequent purulent discharge. This did not respond to the passage of sounds and irrigations. About one year ago he had a series of small pustules (?) on the upper lip and

subsequently "sores" inside the right nostril, which responded to treatment with ointments. One month ago the tip of his nose began to swell, it became reddened and sore.

Examination shows excessive lacrimation of the right eye, with a purulent discharge that may be expressed from the enlarged lower punctum. There is decided redness of the tip of the nose, especially on the right side. This area is indurated but not tender. The right nasal passage is almost occluded by granulation tissue. The remainder of the physical examination gave essentially negative results. Roentgenograms of the chest showed no conclusive evidence of pulmonary parenchymal infiltration, although the hilar shadows were increased. The Wassermann and Kahn reactions were negative. The sedimentation time was within normal limits.

A biopsy was done a week ago. A guinea pig was inoculated with half the tissue, and the rest was prepared for microscopic study. No acid-fast organisms were found on direct examination of the material.

DISCUSSION

There was no discussion of this case.

Lupus Erythematosus Presented by DR A E INGELS

C L, a white woman aged 39, a telegraph operator, came to my office on Dec 16, 1938.

She had always been well until last summer during her vacation, when she sustained a severe sunburn after walking outdoors without a hat all day, in contrast to her previous indoor city life. She states that ever since this time she has not felt well and has had no "pep". The initial severe sunburn cleared, but the nose continued to peel. A fiery red plaque developed on the tip of the nose about the first of November. In a short time it started to weep. The lips and the gums were extremely sore at this time. A superficial ulcer developed on the lower lip and shortly spread over the entire lip. The mouth was treated with gargles during this time, but the gums became more sore and tender.

There were no abnormal physical findings except in the skin. When first seen the nasal lesion consisted of a crusted, highly inflamed and weeping plaque 3 cm in diameter, occupying the tip of the nose. The horny crust could be lifted up with ease, the under surface then showing a dense studding of horny plugs, leaving patent follicles. The lips showed redness, swelling, crusting and superficial ulceration. The mouth had a fetid odor (no bismuth had been given), and swelling and soreness of the gums were seen.

Repeated dark field examinations for *Spirochaeta pallida* have all given negative results. Two Wassermann tests, one performed about the middle of December and one the first of April, gave negative reactions. Two examinations for *Coccidioides immitis* gave negative results. Roentgenograms of the teeth showed no abscesses or devitalized teeth. Roentgenograms of the sinuses were clear. The urine was normal.

Examination of sections showed the epidermis to be normal except for slight intercellular and intracellular edema. The cutis showed rather heavy round cell infiltration, which was centered mainly around the follicles and sweat glands and about the vessels. Both polymorphonuclear leukocytes and lymphocytes were seen. No giant cells, epithelial cells or tubercle formations were present. Dilated sweat glands were observed. Van Gieson and elastic tissue stains showed homogenization, i. e., formation of elastin and colasin. A section stained with Becker's stain showed absence of pigment in the basal cell layer. Horny plugging in some of the hair follicles was seen.

Weekly intramuscular injections of bismuth subsalicylate and iodobismutol and a ketogenic diet have been given. Plasmochin, $\frac{1}{6}$ grain (0.01 Gm) twice daily, has also been given. The patient feels much better. The lesions have improved considerably.

DISCUSSION

DR N N EPSTEIN In addition to lupus erythematosus, I think one of the bullous diseases must be considered The course of the condition will tell the story

DR MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif Is there any history of ingestion of drugs?

DR A E INGELS There is no history of intake of drugs I feel that at present lupus erythematosus is the most tenable diagnosis In addition to the histologic picture, which is consistent with this diagnosis, the clinical behavior of the lesion on the nose seems important

Purpura Annularis Telangiectodes. Presented by DR H J TEMPLETON, Oakland, Calif

H G B, a white man aged 42, consulted me on March 24, 1939, because of coin-sized purpuric rings located on the buttocks and thighs These have been present for about five years

The patient states that the lesions begin as pea-sized pinkish macules which gradually enlarge, clearing in the center to form rings

Inspection reveals a few pea-sized macules and many coin-sized purpuric rings The centers of the ringed lesions show some evidence of atrophy

A blood count showed a hemoglobin content of 80 per cent There were 4,600,000 erythrocytes and 6,850 leukocytes per cubic millimeter A differential count showed 70 per cent polymorphonuclear leukocytes, 24 per cent lymphocytes and 6 per cent mononuclear leukocytes There were 320,000 blood platelets

Histologically there were no noteworthy changes in the epidermis In the pars subpapillaris there was a sharply demarcated cellular infiltrate consisting mostly of lymphocytes Vascular changes were minimal, and there was no free hemorrhage

DISCUSSION

DR L R. TAUSSIG I agree with the diagnosis I think this is a typical case of Majocchi's disease I do not believe that there is a specific histologic picture in this condition

DR EUGEN OSTWALD (by invitation) My associates and I treated some such conditions in Europe by destroying the lesions most annoying to the patient with desiccation, but I should like to know whether Dr Templeton or any of the members has any other suggestion

DR A E INGELS Clinically, I agree with the diagnosis However, I feel that further microscopic study of the sections is needed

DR HIRAM E MILLER This might be another case in which to try snake venom

DR H J TEMPLETON, Oakland, Calif This patient has no subjective complaints, so I do not think one would be justified in using destructive therapy I think instead that the condition should be attacked systemically if treated at all—say with vitamin C

Localized Atrophy of Skin and Subcutaneous Tissue (Hemiatrophia Faciei? Scleroderma?). Presented by DR H V ALLINGTON, Oakland, Calif

A S, a white housewife aged 31, is presented from the Berkeley General Hospital Dermatologic Clinic She was referred to me by Dr Wallace Patch because of areas of atrophy of the skin and subcutaneous tissue The largest one involves the left side of the forehead It extends from the supraorbital ridge as a band 4 or 5 cm wide into the left frontal portion of the scalp Irregular areas continue over the left side near the midline to the occiput Another, 2 to 3 cm in diameter, is present just below and to the right of the external occipital protuberance Other lesions, from 5 to 8 cm in diameter, are present to the left of

the spine of the first dorsal vertebra, over the medial aspect of the left foot and on the lateral surface of the right foot. The lesion on the left side of the forehead and scalp began at the age of 16. The others are relatively inconspicuous, and the date of their onset is not known. The lesions are thought to be slowly increasing in size. The patient remembers no redness, swelling, hardening or pain in the involved areas either before or since the onset. At present there is no notable change in the color of the skin. The atrophy involves both the skin and the subcutaneous tissue. In the scalp the more advanced lesions are shiny and smooth and the hair is absent. There is no palpable infiltration of the margins of the lesions except possibly in the medial margin of the lesion on the forehead, and there it is slight. The areas are slightly hypesthetic, but Dr. Lester Lawrence, who made a neurologic examination, feels that this is due to local atrophy of the sensory apparatus rather than to any disturbance of the regional or central nervous system.

In addition to her cutaneous troubles, the patient has complained of nervousness, constipation, nausea, heartburn, premenstrual pain and hot flashes. Salpingectomy was performed on each side, and oophorectomy on the left side in 1932. There is general dryness of the skin. Pelvic examination by Dr. Harry Aitken revealed a tender mass in the right adnexal region, probably a cystic right ovary.

The basal metabolic rate on Aug. 23, 1938 was -16 per cent. A Kline test on August 20 gave a negative reaction. The sedimentation time on October 17 was three hours (Linzenmeier method).

Roentgenograms of the skull were described by Dr. L. M. Knox as follows:

"There is no evidence of atrophy of the outer table of the skull along the left frontal region. There is nothing to indicate any difference between the left half of the cranium and the right half. However, the areas on the two sides of the midsagittal plane in the parietal regions show a filmy light decalcification in which the normal trabeculation of the bone is absent. This sort of change one sees with Paget's disease of the bone."

Administration of 1 grain (0.06 Gm.) of thyroid daily and injection of gonadotropic substance from the urine of pregnant women have resulted in some improvement of the patient's general condition.

DISCUSSION

DR. J. M. GRAVES: It was almost impossible for me to believe that there was nothing wrong with this woman's skull. The condition seemed to me to be the end result of scleroderma.

DR. C. E. SCHOFF, Sacramento, Calif.: I have a similar case, the patient being a girl whose involvement extends well up into the parietal region. At times the objective symptoms manifest themselves as numerous nodules which appear to be situated in the subcutaneous tissue. The entire area involved extends from the angle of the jaw to the outer margin of the orbit and "fans out" over the temporal, the parietal and the posterior frontal region. When I first saw her, a number of years ago, I made a clinical diagnosis of sarcoid. Subsequently I changed the diagnosis to scleroderma, and more recently I have felt that the proper diagnosis would be hemiatrophy faciei. A point of interest is that during the so-called active stages, when she has been treated with gold sodium thiosulfate, the inflammatory reactions and the nodules disappear.

DR. MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif.: This patient has muscular atrophy. I wonder whether it may be of neurologic origin and a form of hemiatrophy.

DR. HIRAM E. MILLER: I think that this is the usual type of involvement seen in scleroderma of the "en coup de sabre" type.

DR. H. V. ALLINGTON, Oakland, Calif.: A diagnosis of hemiatrophy was considered the most tenable one until it was found that the lesions occurred on both sides of the body.

A Case for Diagnosis (Thickening and Exfoliation of Mucous Membrane of Mouth). Presented by DR H V ALLINGTON, Oakland, Calif

A M, a white man aged 22, presents areas of milky white ragged, sodden, exfoliating oral mucous membrane. The process is maximal on the cheeks, opposite the premolar and molar teeth, but occurs also in places on the lingual, gingival and labial surfaces. It began four or five years ago. It causes no discomfort.

The patient is conscious of biting his cheeks frequently. Whether this habit is the result of the mucosal changes or whether it is a factor in causing them is questionable.

The patient's father is said to have similar lesions in his mouth, which have been present for many years. The patient's general health is good. There are no associated cutaneous lesions. There are numerous amalgam fillings in his teeth. Reactions to patch tests on the skin of the forearm with amalgam and with a 1 per cent ammoniated mercury ointment were absent at forty-eight hours, but strongly positive delayed eczematous reactions developed a week later to both.

A Kline test gave a negative result. A blood count was normal. Microscopic examination and cultural examination failed to reveal yeasts.

The diagnoses considered included intolerance to the mercury in amalgam fillings and hereditary hyperkeratosis and exfoliation of the mucosa.

DISCUSSION

DR N N EPSTEIN. I thought the lesions could not be distinguished from those of leukoplakia or possibly lichen planus.

DR C J LUNSFORD, Oakland, Calif. I saw the patient in the office and thought the condition was most probably lichen planus. Clinical differentiation, however, is very difficult. I did not know that patch tests had been subsequently made.

DR H. J. TEMPLETON, Oakland, Calif. I should have the amalgam fillings taken out of this man's mouth.

DR MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif. I thought of dentifrices, and also that he might have been chewing the area. I have seen a patient with an eruption of the palm and soreness of the mouth after using a proprietary tooth paste (Dr Strasska's). Also, the habit of biting a small excrescence in the mouth might be a factor. Sodium perborate if it is used, will cause whitened areas in the mouth. I think these conditions might be considered rather than leukoplakia.

DR HIRAM E MILLER. The more severe areas on the inner surfaces of the cheeks are directly opposite the amalgam fillings. The lesions have been present for five years and the fillings for six years. If the patient were under my care, I should advise that the fillings be removed.

DR C. E. SCHOFF, Sacramento, Calif. In the patients that I have observed with pseudomembranes due to electrolytic phenomena as described by Lane there has been direct contact between the fillings and the tissue on which the membranes have formed. In this patient I did not see any fillings that were in direct contact with the involved area.

DR H V ALLINGTON, Oakland, Calif. I think this patient's condition is different from ordinary leukoplakia. If a dull curet is run over the area, large chunks can be easily peeled off, and the mucosa beneath is dull red and ragged. The lesion is sheetlike rather than reticular, as in lichen planus.

I have asked the patient to have all the fillings removed and replaced by gold, but he has objected on the grounds of expense.

Urticaria from Cold Presented by DR H V ALLINGTON, Oakland, Calif

W W W, a white University of California student aged 22, has had localized areas of edema following exposure to cold for the past ten years. He associates the onset of this with being struck by a sting ray while surf bathing. This history is indefinite, however.

The intensity of the reaction gradually diminished until two years ago, when it flared up after a severe attack of poison oak dermatitis. At present, exposing

any part of skin to cold results within two or three minutes in a tense swelling limited to the area exposed. There is little change in color, the area being, if anything, paler than normal. Both subjectively and objectively the area feels tense and cold. The reaction begins to disappear in about thirty minutes. There is no general disturbance. For example, swelling of the hands occurs if they are exposed to the wind while riding to school. A cold shower will cause widespread giant urticarial swelling over the trunk and extremities, while a lukewarm or hot one will not. There is no increase in reaction to mechanical stimulation (dermographia), and the skin appears to respond normally to light.

The patient has had no serious illnesses. A weakly positive tuberculin reaction was observed in 1936. Roentgenograms of the chest were normal at that time. On April 11, 1939 the urine was normal and the Kline reaction was negative.

DISCUSSION

DR ERNEST K. STRATTON: The patient states that the attacks of urticaria brought on by exposure to cold date from the time he was wounded by a cold water fish. Perhaps he could be desensitized by injecting small doses of an extract made from this animal.

A Case for Diagnosis Presented by DR CHARLES ALBERT SHUMATE

N. O., a Japanese ranch laborer aged 52, a resident of Yuba County for the past thirty years, was seen by Dr. H. E. Alderson as a private patient.

He presented several dark red, round, slightly elevated nodules 1 cm. in diameter on his neck and left eyebrow and also a series on his left arm. Smaller ones were found on his right arm and trunk. The first nodule appeared on his neck about March 10, 1939.

At Yuba City a local physician gave him sulfanilamide for seven days. He stopped work but was exposed to sun. On about April 3, macular erythematous areas appeared profusely on the hands, face, legs and back. Since the drug was discontinued the erythema has gradually faded.

At present treatment consists of giving sodium salicylate tablets, one every four hours, and the condition has improved without any other treatment.

The patient was healthy and strong up to fourteen years ago, when he first noticed slight atrophy of the left arm. This slowly increased until seven years ago, when he was seen by Dr. Howard Naffziger, who advised removal of abscessed teeth and gave the patient drops to take internally. Dr. Naffziger's diagnosis was "progressive muscular atrophy." The arm has gradually wasted since then and lately has been sore. Otherwise the patient is apparently in good health.

The Wassermann reaction was negative.

DISCUSSION

DR FRANCES TORREY: The lesions are very sensitive to pain.

DR N. N. EPSTEIN: One lesion on the back of the neck seems to me to be fluctuant. If this is true, laboratory studies should be made to rule out fungous disease. I think that the diagnosis can be made only by histologic study and culture.

DR J. M. GRAVES: I think that the condition probably is leprosy.

DR HIRAM E. MILLER: I think it is suggestive of lymphoblastoma.

DR A. E. INGELS: The nerves are greatly thickened on both sides.

DR MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif.: The left ulnar nerve seems to me decidedly atrophic and soft, and the right is thickened and hardened.

DR G. V. KULCHAR: I do not think that the nerves are thickened. The condition looks to me more like a tuberculoid type of leprosy, although it may be lymphoblastoma.

DR MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif.: Leprosy is, I think, the diagnosis most strongly suggested.

LOS ANGELES DERMATOLOGICAL SOCIETY

KENDAL FROST, M D, *Chairman*CHARLES R CASKLY, M D, *Secretary*

May 9, 1939

Parapsoriasis (en plaque type)? Presented by DR NELSON PAUL ANDERSON and DR O M STOUT (by invitation)

N P, a white man aged 48, presents an eruption which began in 1932 as small brown macules on the medial aspects of both thighs. They gradually increased in size and number until the upper parts of both thighs became involved. More recently the medial and posterior aspects of both arms have shown similar lesions. The lesions are light brown slightly erythematous scaling macules which coalesce into large plaques.

The blood count was normal, and urinalysis gave negative results. The Wassermann reactions of the blood and the spinal fluid were positive. The patient has been under treatment for meningovascular syphilis since 1933. Local treatment has consisted of the application of Mook's lotion, salicylic acid and sulfur ammoniated mercury and crude coal tar.

DISCUSSION

DR SAMUEL AYERS JR I think the lesions are compatible with the diagnosis of parapsoriasis en plaques.

DR WILLIAM H GOECKERMAN I agree with the diagnosis.

DR NELSON PAUL ANDERSON I thought it would be interesting to present this patient for the reason that six years ago a biopsy was performed on one of the lesions. A histologic diagnosis was made of parapsoriasis with possible premycotic changes. A recent report from the laboratory was that if the condition clinically is parapsoriasis, histologically it must be a premycosis fungoides because of the presence of considerably more cellular infiltration than is found in the usual case of parapsoriasis. I think that eventually a frank mycosis fungoides will develop. I think this case raises the question whether there is such an entity as parapsoriasis of the en plaque type, particularly in view of the recent work of H Keil (ARCH DERMAT & SYPH 38 545 [Oct] 1938).

A Case for Diagnosis (Papulonecrotic Tuberculid?) Presented by DR H C L LINDSAY

M G, a white woman aged 62 weighs 223 pounds (101.1 Kg). Her arms show many areas about the size of the end of a cigaret which present atrophy and telangiectasia. Laboratory tests revealed nothing abnormal except for the presence of sugar in the urine, and this was not found at every test. The local form of treatment has been calamine lotion.

DISCUSSION

DR SAUL ROBINSON I was thinking of the possibility of neurotic excoriations. She mentioned insect bites which were present from time to time. I noticed that one of the areas was excoriated.

DR C R HALLORAN Though the pigmentation in the scars suggests a papulonecrotic tuberculid, the lesions are distributed over areas easily reached by the patient. I favor the diagnosis of neurotic excoriations.

DR SAMUEL AYRES JR I think that the condition is a little vague. The lesions on the arms appear to be some toxic reaction, such as lichen urticatus. Pruritus is

undoubtedly present I do not think that the itching would be compatible with necrotic tuberculid Tuberculids also would be more apt to occur on the fingers, legs and ears, as well as on the arms Then there is the peculiar telangiectasis on the breast and legs and a slight suggestion of it on the back That also may be some toxic manifestation I do not know whether the two conditions can be tied together I have seen widespread spontaneous telangiectasis associated with chronic sinusitis which seemed to be cleared up on treatment of the latter

DR IRVING BANCROFT This woman has diabetes, and that is sufficient cause for a toxic condition She can scratch and thus produce the scars

DR H C L LINDSAY I believe that the case is one of diabetes in which the patient has itching and produces the lesions by plucking out pieces of flesh The peculiar telangiectases on the ankles and on the breasts are not artefacts The lesions that have healed have telangiectases also

Bowen's Disease (of the Penis). Presented by DR KENDAL FROST and DR O. M STOUT (by invitation)

W M, a white man aged 58, was circumcised at the age of 21, and there occurred an infection and subsequent scar formation Four years ago a small vesicle formed at the edge of the scar, and soon thereafter the area became moist and weeping The area has never healed, in spite of various types of local treatment There has been a gradual increase in the size of the area for the past two years At the present time there is on the ventral surface of the penis a crusted indurated area the size of a quarter The central portion of the area is thicker The periphery is surrounded with small vesicles

The Wassermann reaction of the blood was negative The pathologic diagnosis was epidermoid carcinoma

DISCUSSION

DR NELSON PAUL ANDERSON I think that the condition is one which if it could have been seen one or two years ago would have been diagnosed as erythroplasia The histologic section reveals an epidermoid carcinoma The section presents some of the features of a basal cell epithelioma, but this disease does not occur on the glans penis, and probably Bowen's disease does not either. I think the lesion should be treated radically

DR H C L LINDSAY Does not Paget's disease occur on the penis?

Fixed Arsenical Pigmentation Presented by DR NELSON PAUL ANDERSON and DR O M STOUT (by invitation)

For J D, a white man aged 57, a diagnosis of latent syphilis was made in 1935 His first treatments were weekly injections of mercury On Sept 4, 1936, weekly injections of 0.2 Gm of bismarsen were begun After the nineteenth injection a mild generalized arsenical dermatitis developed, which subsided when the administration of the drug was discontinued, but there remained several reddish brown pigmented macular areas on the thighs and the lower part of the back. These areas have remained about the same

The Wassermann reaction of the blood was 4 plus

DISCUSSION

DR WILLIAM H GOECKERMAN On clinical examination I agree that the condition is a drug eruption, but whether it is due to the arsphenamine I am not prepared to say I can only say that I have not seen a clinical picture like this in cases of fixed arsenical dermatitis Since the patient has been given bismarsen, is it possible, in the light of some of the cases of fixed pigmentation presented in the past, that this peculiar picture may be due to both bismuth and arsenic? The patient gives a history of unusual sensitiveness to sunlight I should accept a diagnosis of fixed drug eruption, but further studies are desirable I suggest patch tests on the pigmented areas

DR C R HALLORAN In the group of cases of pigmented eruptions following treatment with arsenicals and bismuth that Dr Bancroft and I recently reported (*California & West Med*, to be published), we encountered none with this peculiar iodine color. However, there were no cases in the group that we studied in which the eruption followed injections of bismarsen. It may be that this particular drug is in some way associated with the peculiar color.

DR IRVING BANCROFT I have never seen a condition like the one presented in any fixed pigmentation. It seems to me there should be some examinations to see if there is any abnormality of the fat metabolism.

DR A F HALL JR I thought that in view of the peculiar color of the lesions and the fact that the patient was receiving bismarsen when the lesions appeared it would be interesting to give him at intervals injections of neoarsphenamine, a bismuth compound and sulfarsphenamine, to try to determine whether the arsenic, bismuth or sulfur radicals in the bismarsen might be responsible for the peculiar color.

DR C R HALLORAN I do not believe that a therapeutic test would be of great value. We found that new lesions developed in many patients with continuation of the treatment and that new lesions continued to develop in many patients for some time after treatment had been discontinued.

DR O M STOUT (by invitation) The patient has received bismarsen since the onset of the eruption, and it does not affect the lesions. He gives no history of drugs taken by mouth. He is a total abstainer from alcohol.

A Case for Diagnosis (Ainhum? Syphilis? Periarteritis?). Presented by DR S O CHAMBERS and DR A J GRECO (by invitation)

M A C, a Negro aged 49, in 1921 had a penile chancre. Subsequently there was a positive Wassermann reaction. After eight months of antisyphilitic treatment the reaction of his blood was negative, and there was no further treatment until March 20, 1932. He was hospitalized from March 20, 1936 to August 15 for treatment of ulcers of the feet. About 1932 he first noticed thick calluses on the soles and toes. They were soaked and pared off, leaving raw ulcers. Gradually the left great toe sloughed off, leaving a ragged stump. Then the tip of the second toe sloughed off. During 1936 the right great toe became smaller and shorter. On Jan 6, 1937, at a staff conference of the Veterans Administration Facility at West Los Angeles the following diagnoses were made: (1) tabes dorsalis, (2) chronic alcoholism, (3) atrophy of the optic nerve, (4) neurogenic ulcer of the great toe, (5) syphilitic osteoporosis and (6) arthritis of the toes.

The dermatologic condition is associated with the arthritic deformity of the toes. The left great toe, which has been spontaneously amputated at its metatarsophalangeal joint, has left a ragged stump which is covered with thick callous tissue. The second toes have been partially amputated at their distal joints, the left having lost its nail, and the right great toe is shortened. All the other toes are curled on their metatarsal heads, and all show loss of motion and ulcerated callosities on their dorsal surfaces. Arterial pulsations are normal, and the feet and toes are all of normal color and warmth.

In November 1936 tissue was removed from the ulcer of the right great toe, and a histologic diagnosis of obliterative endarteritis suggestive of syphilis was made. From June to November, 1936 the patient received twenty-three intramuscular injections of a bismuth compound, with indifferent results.

Calluses have been softened with salicylic acid plasters applied three times weekly. The treatment has improved the local condition to some extent, so that the patient can now walk fairly well.

Recently injections of a bismuth compound have been resumed.

DISCUSSION

DR WILLIAM H GOECKERMAN There are a number of possibilities, some probably outside the field of dermatology. I think that there is a trophic dis-

turbance, in which the nervous system is of course involved. I thought at first that the condition possibly might be leprosy, but further examination did not yield corroborative evidence. It is striking that leprosy is as capable of producing variegated clinical pictures as syphilis and tuberculosis and that it need not present a textbook picture. A section of nerve tissue for microscopic study is desirable. I do not believe that the condition is anhidrosis.

I think that a careful neurologic examination should be made, since the patient complains of numbness of the soles and is seemingly insensitive to pin tests. I could not see much evidence for a vasomotor disturbance, such as Raynaud's disease, not even one that may have run its active course.

DR NELSON PAUL ANDERSON. It is my impression that when anhidrosis causes amputation of the toes it usually involves the little toe and that if multiple toes are involved the fourth toe is the one next affected. I agree with Dr Goeckerman that the patient should be examined carefully with a view to the possibility of leprosy. I received the impression that he had a large ulnar nerve on the left side, although the one on the right was not so prominent. I think it would be well to perform a biopsy of nerve tissue. Syringomyelia can produce this picture, and I should consider syringomyelia or leprosy rather than syphilis.

DR SAMUEL AYRES JR. It was not clear to me whether amputation of the toes occurred because of the development of the constriction ring or whether the terminal phalanges became gangrenous and fell off. If there is not any history of a characteristic constriction ring I should be inclined to regard the condition as an endarteritis, possibly of syphilitic origin. I gathered that there was no clinical or spinal fluid evidence of tabes.

PHILADELPHIA DERMATOLOGICAL SOCIETY

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Sept 15, 1939

Universal Depigmentation of the Skin, with Areas of Hyperpigmentation Presented by DR HOWARD EARL TWINING

J. T., a Negro aged 50, in 1917 first noticed on his chin and hands white spots which gradually became universal. In the summer of 1938 the exposed areas of the skin became blistered after exposure to the sun, after which they became hyperpigmented. The entire cutaneous surface is now white except for the areas of hyperpigmentation on the face, hands and arms.

DISCUSSION

DR JOHN H. STOKES. I think this patient is interesting because he demonstrates, if his statement about his original color is correct, that there is really hyperpigmentation associated with depigmentation of the skin. Not infrequently it is said that hyperpigmentation is an optical illusion based on contrast between the depigmented skin and the normally pigmented skin, possibly accentuated by exposure to sunlight. But this man has extremely dark spots which clearly illustrate the marked hyperpigmentation phase of the leukoderma picture.

DR JACQUES P. GUEQUIERRE. The patient also stated that he worked in a steel mill and that some of the areas of hyperpigmentation are where pieces of steel and slag struck his skin.

A Case for Diagnosis (Erythema Multiforme? Pemphigus? Dermatitis Herpetiformis?) Presented by DR ABRAHAM STRAUSS

B. B., a white boy aged 16, presents a more or less generalized wheal-like eruption, with some of the lesions surmounted by blebs and others by pustules.

There is considerable itching, and at times the patient has had mild fever. He was first seen on April 4, 1939, with a severe dermatophytosis of the hands, associated with pyoderma and considerable edema. There was slight fever and axillary lymphangitis. This condition cleared up except for some lesions around the finger nails. The present condition began four weeks ago with blebs under the upper part of the right arm and then gradually spread. Fungi were found by culture and microscopic examination during the first attack, but none have been found in the present one. A blood count showed 75 per cent hemoglobin, 3,800,000 erythrocytes per cubic millimeter and 11,800 leukocytes per cubic millimeter. Soothing lotions and sulfanilamide have been administered, with apparent control of the lesions.

DISCUSSION

DR. ERICH URBACH (by invitation) It seems to me that this condition is a bacterid.

DR. JOHN H. STOKES I think the condition is the erythema multiforme or pemphigoid or pemphigus-like type of bacterid, which has been described by Bruusgaard (*Brit J Dermat* 34:150 [May] 1922). He reported a case in which a typical erythema nodosum was traced directly to a fungous infection, kerion celsi of the skin. In fact, fungi were recovered, I believe, from the patient's blood. I cannot see why it is so difficult to imagine a secondary dermatitis, such as so commonly occurs after sensitization by fungi. The second phase may be more pustular than the first. What interested me most was the statement that "cauliflower" ears developed about four days after the sulfanilamide therapy was stopped. Dr. Flood and I have been impressed with that peculiarity of the effect of sulfanilamide. The drug appears to be, for dermatologic lesions, bacteriostatic rather than bactericidal. The cessation of the administration of the drug may be followed by a relapse of the original eruption. I have a feeling that some conditions diagnosed as toxic eruptions due to sulfanilamide are really violent flares on the order of a syphilitic relapse. In a case in which there is diminished resistance and no developed defense, a relapse may perhaps occur and not a toxic eruption due to sulfanilamide. In this case the development of the condition of the ears and the erythema-multiforme-like eruptions on the face four days after the stopping of the ingestion of sulfanilamide seems to me deserving of investigation from that standpoint. There may be an interplay between virus infections and fungous infections and between fungous infections and superimposed virus infection. Possibly some of the conversion forms of streptococci, which become so small that they are filter passing, are the bacterid agents. One may fail to find a certain organism, and cultures may frequently fail to give positive results, because the organism has passed into this different form. I think that here is a field for investigation which may yield observations of importance in the future.

DR. ABRAM STRAUSS Will further administration of sulfanilamide aggravate or help the patient under discussion?

DR. JOHN H. STOKES I think it would be well to try it again. The action of the drug may be controlled by watching the blood count. I do not think the drug should be given to the boy unless he is hospitalized and the effect on the blood is observed by daily counts.

DR. HERMAN BEERMAN This case reminds me of one that Dr. Fondé and Dr. Goldberg described, in which a patient with lymphogranuloma venereum was treated with an antimony compound (*ARCH DERMAT & SYPH* 34:478 [Sept] 1936).

A Distinctive Type of Tuberculosis in the Negro Associated with Tuberculous Keratouveitis Presented by DR. ELMER R. GROSS, Wilmington, Del.

H. G., a Negress aged 40, was first seen in March 1935, with uveitis of both eyes. The Wassermann reaction of the blood was strongly positive. The vision was 6/9 in the right eye and 6/15 in the left eye. She was given fifty injections of

a bismuth compound, thirty-six injections of neoarsphenamine and oral doses of potassium iodide between March 1935 and November 1937. In August 1936 the Wassermann reaction of the blood was negative, and tests of the spinal fluid gave negative results. In November 1936 a cutaneous lesion appeared on the right thigh and was followed by the gradual development of lesions elsewhere.

Examination of both extensor surfaces of the legs reveals discoid elevated and infiltrated plaques about 2 cm in diameter, some of which are smooth, others atrophic and depressed and others scaly. There are also some plaques on the back and a few on the lower side of the chest following the lines of cleavage. There are a few split pea-sized lesions on the face and the atrophic remains of lesions on the scalp. The patient is well developed but poorly nourished. Roentgenograms showed evidence of pulmonary tuberculosis but no changes in the bones of the hands. Examination with a slit lamp revealed hazy corneas and numerous large and small mutton fat grayish deposits on their posterior surfaces. The von Pirquet reaction in November 1937 with a dilution of 1:10,000 was negative. The reaction in June 1939 with dilutions of 1:10,000 and 1:1,000 was negative. On April 17, 1939 the vision in the left eye was 6/60 and in the right eye was limited to light perception. Histologic examination of a cutaneous lesion revealed typical tuberculous architecture.

DISCUSSION

DR EDWARD F. CORSON: Dr. Ludy had a patient with a similar type of cutaneous eruption and with one eye blind and vision in the other was limited to light perception. This form of tuberculosis is commonly observed in the Negro. Often a depigmented ring surrounds a granulomatous lesion. One sees the same rounded patches as this woman shows on the cheeks. The condition is not lupus vulgaris, tuberculosis verrucosa cutis or scrofuloderma, and I should appreciate knowing in what category to include it.

DR JOSEPH V. KLAUDER: Dr. Weidman and I have regarded this as a distinct type of tuberculosis in the Negro. Others think that it is another expression of Schaumann's disease. If the latter conception is the correct one, I think the condition should be regarded as an unusual expression of Schaumann's disease.

Lupus Erythematosus Presented by **DR ELMER R. GROSS**, Wilmington, Del.

E. S., a white man aged 29, was presented at a previous meeting (Jan. 21, 1938) with the diagnosis of lupus erythematosus or sarcoid. He is now presented with the diagnosis of lupus erythematosus, the histologic report and clinical improvement being consistent with this diagnosis. He now presents a disappearing remnant of a lesion on the right supraorbital ridge and a dime-sized lesion on the left supraorbital ridge. The patient was treated with two courses of a bismuth preparation, a saltless diet and hygienic measures.

Nickel Dermatitis (from Spectacle Frames) Presented by **DR ELMER R. GROSS**, Wilmington, Del.

M. P., a white woman aged 43, appearing to be in good general health, presents a subacute dermatitis of both supraorbital regions and along the line of the temples and the ear pieces of the glasses. The upper part of the chest is the site of a similar eruption. The result of a patch test made with scrapings from her spectacle frames was positive.

DISCUSSION

DR JOHN H. STOKES: I think some persons hesitated to accept the sensitization conception of this condition because of the eruption on the chest. I have noticed the possibility of the association of nickel with pyogenic infection. The pyogenic infection may lead to nickel sensitization, and the nickel sensitization can certainly lead to an overwhelming spread of the original pyogenic infection, extending far

beyond the area in contact with the nickel I have seen the contact of a nickel truss in the groin result in an extensive flare Spectacles can cause the same result The process will extend down the nose and out on the face, and then isolated pustules, extensions of the process, may be scattered over the shoulders That, I should say, is the probable explanation of the eruption on this woman's chest

DR THOMAS BUTTERWORTH, Reading Another explanation for the eruption on the chests of these patients was illustrated by a patient I saw recently She had nickel dermatitis on her head where the skin came in contact with her glasses and on her chest where the skin came in contact with the little nickel-plated piece of metal used in adjusting the length of the straps of her slip There was an area of dermatitis possibly 2 to 3 inches (5 to 7.5 cm) in diameter on the upper part of the pectoral region of each side The same patient showed dermatitis over the region in contact with the white gold band of her wrist watch and two palm-sized areas of inflammation on the front and back of the thighs where the nickel of the garters came in contact with the skin It might be wise to check as to whether nickel of an adjustable band on this patient's slip is the source of the eruption on her chest

Primary Atrophy of the Optic Nerve, Juvenile Tabes Dorsalis Presented by DR MARJORY HARDY, Norristown, Pa (by invitation)

L C, a Negress aged 19, was first seen in June 1939, when she said her vision had been getting worse for the past two months Her vision on June 1, 1939, was 6/12 in the right eye, and all she could see with the left eye was movements of the hand On June 17, 1939, it was 6/15 plus 2 in the right eye, and the left eye was blind Her facies is normal, and her joints and tibias are normal She has an open bite The teeth are dwarfed, with some appearing deciduous The upper central incisors are dwarfed but are not of the hutchinsonian type On the left side there are mulberry molars in both the upper and the lower jaw The pupils are irregular and do not react to light The patellar reflexes are absent, and the Romberg sign is positive The Wassermann reaction of the blood was positive The examination of the cerebrospinal fluid showed 133 lymphocytes per cubic millimeter, reaction for globulin, weakly positive, Meinicke reaction, strongly positive, Wassermann reaction, strongly positive, and colloidal gold curve, 1233100000 The patient was inoculated with malaria organisms, but no rise in temperature or chills followed She has received neoarsphenamine and injections of a bismuth preparation

DISCUSSION

DR JOHN H STOKES I wish to comment on the extraordinary behavior of juvenile tabes in some cases This point was demonstrated to me by a patient whom I first saw nearly twenty years ago His father had neurosyphilis, his mother had latent syphilis, his brother had all the stigmas of congenital syphilis, and this boy had tabes with gastric crises which frequently taxed all my resources to the limit to pull him through alive Now he is grown and married and has a child The sole residue of his gastric crises is what I think is a fear neurosis, which causes him to be nauseated every morning at an appointed hour and for an appointed time, after which he is able to rise and go about his business No fewer than eight Charcot joints have developed, his feet have spread into flippers, he has more Charcot toes than normal toes, not counting the amputations, at least seven vertebrae have been almost completely absorbed by Charcot changes in his spine, his deep reflexes are still present, he still has libido and potentia, but he has lost the stereognostic sense in his hands, so that he cannot distinguish nickels from quarters and consequently cannot make change Apart from these disturbances, he is a living member of society His health was nearly ruined recently by his driving to the San Francisco Fair from the city in South Dakota in which he lives He drove 7,000 miles over roads of unparalleled roughness, because he wanted to see the mountains Dr George Wilson, the neurologist, said that this experience left him nervously collapsed, but his peripheral nervous changes, numbness and paresthesias are not

ascribable to irritation of the dorsal roots or to any effect from his Charcot spine whatever. He thinks these processes are periplieral and that the patient can be materially improved by large doses of vitamin B₁. The man is now about 32 years of age, and apart from some stormy episodes has managed to weather juvenile tabes that started in the second year of his life.

DR JOSEPH V. KLAUDER: The fact that the patient presented is a Negro is of interest. I cannot recall having seen juvenile tabes in a Negro. One may question whether the infection is congenital. The age would suggest this origin, but perhaps less so in the Negro race. I think the open bite she presents is definite evidence of congenital syphilis. It is the only structural abnormality she has which is characteristic of the so-called stigmas of congenital syphilis. I think the open bite is perhaps the second most significant dental abnormality found in congenital syphilis. It is not so significant as Hutchinson's teeth, but is more significant than mulberry molars. The prognosis of the atrophy of her optic nerve is not necessarily bad, since malaria therapy may save the vision in her good eye. Since she is a Negress, it is questionable whether she can be inoculated with malaria successfully. If she cannot, she should receive mechanical fever therapy.

Darier's Disease, with Possible Nevroid Changes on the Forehead Presented by **DR HAROLD M. JOHNSON** (by invitation)

M. G., a white man aged 43, well developed, dusky in appearance but apparently in good health, presents a leonine expression because of the infiltration and induration of the supraciliary folds and frontal area of the head. There is a vegetative fungoid lesion 4 cm. in diameter on the right side of the forehead. Several pedunculated lesions 2 by 3 cm. in diameter are scattered over the scalp. Both retroauricular folds have hyperplastic vegetative lesions that almost completely obliterate the spaces. The face is indurated with hyperkeratotic nodules, giving the leonine expression. On the back are confluent keratotic papules. There are many keratotic lesions scattered over the scapular and infrascapular areas, and they are somewhat greasy to touch. These lesions become less numerous toward the sacral region. There are similar hyperkeratotic papules and plaques on the sternal and inframammary regions. The groin presents coalescence of the papules and a purulent exudate. In the intergluteal fold is a large cauliflower-like lesion. The legs, palms and soles are relatively uninvolved. The dorsa of the hands are roughened and keratotic. Seventeen years ago the patient had a "boil on the rectum," which developed into a large ulcer and opened and drained for several years. In 1932 he noticed small vesicles and papules on the lower part of the sacral region. These gradually increased in size and number and spread up the back. The lesions were intensely pruritic and were worse in summer. Several years later his thorax became involved. Five years ago he noticed two small pustules on the side of his nose, which he frequently squeezed with his fingers. Later, pruritic pustules appeared on the forehead and the cheeks. The forehead has become involved only during the past two years. The retroauricular areas have become thickened and hyperplastic during the last year. In spite of treatment the disease has progressed.

DISCUSSION

DR JOHN H. STOKES: I have done some thinking about this case, without arriving at any satisfactory conclusion. I happened coincidentally to see what might be thought of as the beginning of such a process in a young man with verruciform epidermal dysplasia. I wonder whether this man might have some type of dysplasia which might be completely blanketed by the Darier's disease. I shall have to accept it as Darier's disease on the basis of the histologic observations and say that there is something uncomfortably nevus-like about the appearance of the facial lesions and that he may have an epidermal dysplasia of some sort or even some type of fat gland nevus.

DR THOMAS BUTTERWORTH, Reading: This is a typical example of Darier's disease, showing the pronounced scaly papular lesions of the scalp without loss of

hair, the keratosis of the backs of the hands, the diffuse yellowish keratotic thickening of the palms and soles and the fungating lesions in the groins and between the buttocks. A brother has a similar condition, and a sister did not have the disease. The patient cannot give any history of his parents, because his mother died while he was young and he has seen his father only once in his life. Involvement of 66 per cent of the sibship is in accordance with the dominant inheritance characteristic of Darier's disease, in which the theoretic incidence would be 50 per cent.

Late Secondary Syphilis with Pyogenic Infection and Syphilitic Dactylitis.

Presented by DR MARJORY HARDY, Norristown, Pa (by invitation)

A M, a white woman aged 28, presents an ulcerated lesion 1 cm in diameter, covered with a grayish membrane, on the right side of the soft palate. There are many heavily crusted lesions on the arms, legs, trunk and face. These vary in size from 0.5 to 5 cm. Some of them are dry, some are surrounded by an area of redness, and some are indurated and have a punched-out appearance. There is a hard papule on the right ankle. On Aug 29, 1939 the patient had a sore throat, headache and chill, three weeks previously a generalized eruption had developed, and about August 15 the right eye had become inflamed. The patient's temperature was slightly elevated. Just prior to the patient's admission a window fell on the fourth finger of her left hand. A roentgenogram showed a fracture, advanced osteomyelitis involving the distal phalanx and a considerable amount of bone destruction. The Wassermann reaction of the blood was strongly positive. She has had only one injection each of a bismuth compound and of neoarsphenamine.

DISCUSSION

DR DONALD M PILLSBURY. On morphologic grounds, it is much more likely that this condition is either iododerma or bromoderma. The patient stated that she takes bromo seltzer once a week and took some just previous to the onset of this condition. The lesions are highly inflammatory, and those over the legs are granulating and show a tendency to ulcerate, some of the lesions on the face are button-like and pustular. More proof is needed to decide whether the condition is late secondary syphilis.

DR JOSEPH V KLAUDER. The lesions are not by any means typical of an eruption due to secondary syphilis. I think that diagnosis was based on the fact that syphilis is apparently definitely established by the appearance of the throat and by the results of serologic tests. Some of the lesions are definitely infiltrated. There is one on the sole which is certainly suggestive of syphilis. The smooth surface does not suggest a bromoderma, but the ulcerating lesions on the legs, I think, do. There are some lesions with central ulceration and others with a pyogenic crust.

Trichomycosis Axillaris Flava Associated with Alopecia Prematura, Alopecia Areata (Chin) and Fragilitas Crinium (Eyebrows and Upper Lip). Presented by DR REUBEN FRIEDMAN

H N, a white man aged 21, presents on the scalp an abundance of thick black hairs, many of which, however, are easily loosened and extracted on running one's hand through them with gentle traction. The removed hairs reveal no gross abnormalities. The eyebrows are thinned, and some of the hairs are broken, none have nodes. The skin of the axillas presents a thinning of the hair, and many of the hairs present irregular firm yellowish nodular masses along and either partly or entirely surrounding the shafts. There is also splitting of the free ends of some of the axillary hairs. There is no similar involvement of the pubic hairs, although some of them are extracted with ease. The hair on the chest is thinned. The serologic reactions of the blood were negative. This patient is presented on account of the unusual association of four different types of hair lesions (in other words, multiple trichopathies), which according to reports in literature is not uncommon. Lane (*J Cutan Dis* 39:387, 1919) reported having found 51 instances in an examina-

tion of 128 men drafted for the army That would make an average of 2 in every 5 adult males It seems to me, however, that this is a proportion far greater than is ordinarily encountered

DR ERICH URBACH (by invitation) I should not say that 2 of every 5 males abroad have this condition, but I should say that one could see it nearly every day if one were interested in looking for it It occurs especially in tuberculous persons

Pityriasis Rosea in an Infant Presented by DR JOSEPH V KLAUDER

C G, a Negro child aged 6 months, presents scaly lesions varying in size from 1 to 2 cm distributed over the upper part of the back, the sides of the nose and the right side of the face The condition began three weeks ago on the right side of the face and then appeared on the back and neck There are no subjective symptoms

DISCUSSION

DR DONALD M PILLSBURY This pityriasis-rosea-like eruption is commonly encountered, but more frequently in Negro children I see many examples at the Children's Hospital I diagnose the eruption as a superficial type of ringworm infection but have never been able to prove the fungous origin I believe the eruption is related to *achromia parasitica*, and this child has some depigmentation round the hairline I think this condition is a common dermatosis I do not know exactly what it is but I feel certain that it is not pityriasis rosea

DR JACQUES P GUEQUIERRE I did not think the patient had pityriasis rosea I have never found fungi in this condition

DR JOSEPH V KLAUDER It is unusual to see pityriasis rosea in an infant. The condition to which Dr Pillsbury refers is not likely to present so many lesions as does the eruption in this patient Moreover, in that condition the lesions do not follow the lines of cleavage of the skin as they do in this patient It is this feature that suggests pityriasis rosea

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PYODERMA FACIALE

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ROCHESTER, MINN

Since 1933, out of a series of over 1,600 cases of acne in women more than 15 years of age, we have been able to collect 13 instances of an unusual pyodermic process localized on the face. Reports in the available literature and in standard textbooks on dermatology defining this condition are conspicuous by their absence, although a few cases somewhat similar to ours, which we shall discuss subsequently, have been recorded.

This condition, to which we have assigned the term "pyoderma faciale," is a cutaneous disease characterized by a sudden, fulminating onset of pyoderma in young women who are usually in their early twenties. It is localized definitely on the face—the chin, cheeks and forehead bearing the brunt of the attack. A history of clinical signs of previous or associated acne vulgaris cannot be elicited from more than half the patients.

SYMPTOMS

The disease is characterized by an intense reddish to cyanotic erythema extending over the involved portions of the face, with superficial and deep abscesses (fig 1 A) and deep cystic structures.

The abscesses, many of which are linear in outline, are connected with one another through communicating channels or sinus tracts. On evacuation of the contents of the abscesses, a profuse amount of greenish yellow purulent material, sometimes fluid-like in consistency, is obtained. From the older cystic cavities a thin, yellow oily substance may be expressed. The extent of the pyoderma may increase as healing begins (fig 1 B).

The borders of the processes are sharply demarcated from the normal skin (fig 2). Seborrheic characteristics of the scalp and other regions and evidence of acne vulgaris on the skin of the face or chest

From the Section on Dermatology and Syphilology, the Mayo Clinic



Fig 1 (case 5) —In *A* are seen superficial and deep abscesses connected with each other and absence of comedos, *B* shows the appearance two months later



Fig 2 (case 9) —The involvement of the central portion of the face is shown by sharp demarcation from the normal skin. Note the resemblance to vegetative iododerma or bromoderma

are usually absent, or present in a minimal degree. The face may appear to be puffy. Old and new abscesses are frequently present in the same patient. Linear keloidal scars and keloidal retraction of the active abscesses may be prominent features (fig 3).

There is no apparent predilection for any certain type of physique, the disease as we observed it affected sthenic and hypersthenic women as well as asthenic women. Prior to the onset of pyoderma, the patients, with few exceptions, considered themselves to be in good health. In only 1 instance, case 1 in our series, was there any evidence of pre-existing ill health. No history of previous loss in weight, previous



Fig 3 (case 12) —Keloidal scarring and linear abscess

febrile reaction or previous infectious disease was elicited from the patients we observed.

Constitutional symptoms usually are absent, there may be a slight associated loss in weight, and many patients had low grade anemia. A febrile reaction was noted in only 1 instance (case 10). A loss of vigor and vitality was complained of only occasionally, and then early in the course of the disease.

The nosologic category of this condition is indistinct, yet it has many characteristics similar to those of *perifolliculitis capitis abscedens et suffodiens* (dissecting cellulitis of the scalp). When compared with the *acnes*, this type of pyoderma has more features in common with a severe grade of *acne cachecticorum* than with *acne conglobata*. It

must be remembered that these two types of "acne" have certain characteristics in common, a point which has been emphasized recently by Michelson and Allen¹ in regard to acne conglobata and dissecting cellulitis of the scalp

REVIEW OF CASES IN THE LITERATURE

In 1916 Trimble² presented before the New York Dermatological Society a woman 30 years of age who until three months previously had had a smooth, clear skin. After a facial massage, most of the sebaceous glands in her face became inflamed and infected. This condition was succeeded by disseminated scarring. The case presented by Trimble differed from our cases in that the condition followed a massage, an activating process which did not occur among the patients in our series or among the few patients reported on in the literature.

Fuhs³ in 1927 presented in Vienna a 19 year old girl who for a little more than two years had a mild acne, which in the last two month period developed into a "peculiar acne indurata and phlegmonosa." The lesions were localized on the middle parts of the face—the forehead, nose, chin and cheeks—and were sharply demarcated from the normal skin. The lesions were confluent, with perifollicular nodules and nodes and a central pustule. There were multiple softenings suggestive of sebaceous cysts. The specimen taken for biopsy revealed the presence of non-specific inflammation, with formation of an abscess and partial destruction of the follicles in the cutis.

A contracture of the left hip joint, resulting from a draining tuberculous coxitis, was present. Stains for *Mycobacterium tuberculosis* applied to specimens taken from the lesions of the face disclosed no acid-fast organisms, although the reaction to the Pirquet test was strongly positive and the Moro reaction, according to Fuhs, revealed a distinct exacerbation of the inflammatory phenomena in the focus of the disease. Clinical and roentgen examination of the lungs gave negative results for tuberculosis.

Kreibich⁴ described in 1931 as acne conglobata a condition which was etiologically and clinically obscure. The patient was a young girl who was employed in a printing establishment. Restricted to the nose and the adjoining portions of the cheeks were large abscesses, which recurred after incision. There were communications present, connect-

1 Michelson, H. E., and Allen, P. K. Acne Conglobata, *Arch. Dermat. & Syph.* **23**: 49 (Jan.) 1931.

2 Trimble. Acne with Unusual Scarring, *J. Cutan. Dis.* **34**: 766 (Oct.) 1916.

3 Fuhs. Eigenartige Acne indurata und phlegmonosa, *Zentralbl. f. Haut- u. Geschlechtskr.* **23**: 624, 1927.

4 Kreibich. Acne conglobata, *Zentralbl. f. Haut- u. Geschlechtskr.* **38**: 297. 1931.

ing these abscesses with one another and seeming to have a follicular concentration. The characteristic signs of acne rosacea, acne vulgaris and seborrheic eczema were missing.

In 1934 Jamieson⁵ presented before the Detroit Dermatological Society for diagnosis the case of a woman 31 years old who ten years previously had had mild pulmonary tuberculosis. In 1930 she had a mild acne rosacea of six months' duration, and there was a slight recurrence in 1931. A thyroidectomy had been done in January 1933. In April 1933 a group of deep-seated, bluish red acneform lesions developed, appearing on the right cheek and on the right sides of the chin and forehead. Roentgenotherapy was of no benefit, but the lesions healed slowly after drainage. The histologic examination made at the University of Michigan was reported to show evidence of the presence of a chronic infective granuloma, probably tuberculous. The clinical impression was, however, that the condition this patient had was not tuberculosis.

In the discussion of Jamieson's patient Wile stated

For many years dermatologists have been calling eruptions of this type cystic acne. The majority of the cases, however, do not conform to the criteria for ordinary acne. In the first place, they occur in older persons, mostly women, many of whom are married. The onset is usually abrupt, in contrast to that of acne which develops in adolescence.

Many of the patients observed by my associates and me have had a perfectly clear skin up to a short time before the eruption was at its worst. There are few or no comedos. The condition progresses rapidly to the formation of large confluent abscesses much like the cold abscesses of tuberculosis.

Wile stated the belief that such conditions are characterized by a typical tuberculoid structure. In the specimens from 2 patients which we have been able to study histologically, we have not been able to demonstrate a tuberculoid structure. Hasley, also in discussing Jamieson's patient, stated that he had encountered several similar conditions, all afflicting patients past the age of 20 who exhibited evidence of old, calcified pulmonary tuberculosis.

One of us (O'Leary⁶) presented before the Minnesota Dermatological Society in 1934 the first patient of our series. We shall report 4 cases in detail and shall give only a brief tabular summary (table 1) of the observations in the remaining 9 cases.

⁵ Jamieson, R. C. A Case for Diagnosis (Cystic Acne? Tuberculous Granuloma?), *Arch Dermat & Syph* 30 162 (July) 1934.

⁶ O'Leary, P. A. Acne Indurata. Destructive Arthritis of the Right Wrist, Tuberculosis? *Arch Dermat & Syph* 31 407 (March) 1935.

REPORT OF CASES OBSERVED

CASE 1—An unmarried white woman 36 years old entered the Mayo Clinic in April 1934, complaining of arthritis of the right wrist and severe pustular eruption of the face of six months' duration. The family history indicated that her father had had pulmonary tuberculosis. The patient's history, other than the presenting complaint, was essentially insignificant. The presenting purulent eruption had appeared on her chin six months previously, and in a few weeks' time had spread to involve both cheeks. Within the three or four months prior to admission there had been little if any progression of the disease.

Examination showed her to be of the slender, pale asthenic type. Her physical status was essentially normal except for edema and pain on motion of the

Clinical and Laboratory Summary of 13 Cases of Proderma Faciale

| Case | Age of Patient | Duration Months | History of Tuberculosis in Family | Previous Ache | Seborrhea | Comedos | Menstrual Abnormalities or Change | Tooth in Teeth or Tonsils | Anemia | Hemoglobin in Gm per 100 Cc of Blood | Leukocytes | Basal Metabolic Rate | Tuberculin Reaction | Culture |
|------|----------------|-----------------|-----------------------------------|---------------|-----------|---------|-----------------------------------|---------------------------|--------|--------------------------------------|------------|----------------------|---------------------|---------|
| 1 | 36 | 6 | + | + | — | Occ § | — | — | + | 12.0 | 14,200 | +2 | — | — |
| 2 | 25 | 2 | — | + | — | — | — | — | — | 14.3 | 7,600 | —13 | — | — |
| 3 | 24 | 8 | — | — | — | — | — | + | + | 11.9 | 10,200 | —7 | — | — |
| 4 | 21 | 1 | — | — | + | — | + | + | + | 9.1 | — | 0 | — | — |
| 5 | 29 | 1 | — | — | + | Occ § | — | — | + | 10.0 | — | +13* | — | —† |
| 6 | 21 | 12 | — | — | — | — | + | — | — | 15.9 | 11,600 | —10 | — | — |
| 7 | 30 | 12 | — | + | + | — | + | + | + | 12.9 | 8,900 | +2 | — | — |
| 8 | 24 | 5 | — | — | + | — | — | + | + | 10.2 | 8,000 | —2 | — | — |
| 9 | 18 | ? | — | — | — | — | — | — | — | — | — | —1 | — | — |
| 10 | 24 | 1† | — | + | — | — | + | — | + | 11.0 | 10,700 | +7 | — | — |
| 11 | 30 | 2 | — | — | + | — | — | + | + | 11.6 | 6,500 | —1 | — | — |
| 12 | 17 | 5 | — | — | + | + | + | — | + | 12.3 | — | +2 | + | — |
| 13 | 31 | 12 | — | — | + | — | — | + | — | 14.4 | 6,000 | — | — | — |

* After administration of thyroid

† Blood culture

‡ Recurrence

§ Occasional

right wrist. Roentgenologic examination of the wrist disclosed destructive arthritis, probably tuberculous. Only a few comedos were present, and these were situated in areas unaffected by the dermatosis. Examination of the chin and cheeks revealed communicating, undermining, deep and indurated livid abscesses, with sharply defined demarcation from the surrounding normal skin. There were several draining orifices. The regions involved appeared to be edematous, and the surface was smooth except where crusts, formed as a result of drainage, were found.

The value for hemoglobin was reported as 12 Gm per hundred cubic centimeters of whole blood, and leukocytes numbered 14,000 per cubic millimeter. Results of roentgenologic examination of the thorax and of the teeth were reported to be negative. The basal metabolic rate was reported as +2 per cent. An incised abscess yielded a micrococcic growth which was regarded as a contaminant.

When this patient was seen again almost a year later, some scarring from the previous lesions was present, but no signs of active lesions were noted. We also heard from her in May 1937, up to which time she said there had been no recurrence.

CASE 2—A single white woman 25 years old came to the clinic in August 1935, presenting a facial pyoderma of two months' duration. Her family history revealed nothing relevant to her present condition. Her general health always had been good. Since the age of 12 she had had a moderate degree of acne vulgaris of the face, chest and back. Much treatment had been administered for this condition without benefit. In June 1935, large red elevated, undermined plaques composed of numerous pustules and deep abscesses had formed rapidly on the patient's cheeks, forehead, chin and neck. Linear cystic cavities connecting one with another were present. The abscesses would open spontaneously and drain thick creamy pus.

Examination revealed large livid to erythematous elevated plaques, containing indurated abscesses and large pustules on the chin, cheeks and forehead. The abscesses communicated with each other. On the upper portion of the neck were large bandlike, linear cystic cavities, which contained a thin, yellow serous fluid. On the face were numerous small depressed scars, probably representing the residua of previous acne vulgaris. There were no associated comedos and no seborrhea of the scalp.

Results of the physical examination were essentially negative. Results of roentgenologic examination of the thorax were reported as negative. Examination of the blood showed the following: hemoglobin, 14.3 Gm per hundred cubic centimeters of whole blood, and leukocytes, 7,600 per cubic millimeter. The basal metabolic rate was —13 per cent.

In November 1936 the patient wrote to us, stating that she had had no further difficulty with her skin.

CASE 3—A single white woman 24 years old had had a severe pyodermic process on the face for the eight months prior to her admission, and it was for this reason that she came to the clinic in August 1934. In January 1934 erythematous hard nodules had developed on the right cheek, they broke down and discharged pus. There had been no improvement after incision and drainage of the nodules and the use of ultraviolet rays.

One month later, a similar process had appeared on the left cheek and forehead. The patient had received two roentgen ray treatments in February, after which the involved portions became very edematous and numerous pustules and deep, indurated abscesses developed. There was no pain or tenderness in the process.

In May 1934 she had been hospitalized for three weeks because of an unexplained febrile period, during which her temperature increased to 103 F (39.4 C). Since that period, there had been an extensive spread to the chin and the lower part of the face, despite treatment. She had been under the care of a competent dermatologist prior to her admission to the clinic, and a specimen for biopsy had been removed by him and submitted to two general pathologists and two dermatopathologists for diagnosis. Each separately had reported the sections as having a tuberculoid structure. The patient's attending dermatologist, however, had not agreed with this diagnosis, and we also were reluctant to accept the histologic observations as evidence that this young woman had a tuberculous dermatosis.

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Clinical and Laboratory Summary of 13 Cases of Pyoderma Faciale

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|------|----------------|------------------|-----------------------------------|---------------|-----------|---------|-----------------------------------|--------------------------|--------|--------------------------------------|------------|----------------------|---------------------|---------|
| 1 | 36 | 6 | + | + | — | Occ § | — | — | + | 12.0 | 14,200 | + 2 | — | — |
| 2 | 23 | 2 | — | + | — | — | — | — | — | 14.3 | 7,600 | —13 | — | — |
| 3 | 24 | 8 | — | — | — | — | — | + | + | 11.9 | 10,200 | — 7 | — | — |
| 4 | 21 | 1 | — | — | + | — | + | + | + | 9.1 | — | 0 | — | — |
| 5 | 29 | 1 | + | — | + | Occ § | — | — | + | 10.0 | — | +13* | — | —† |
| 6 | 21 | 12 | — | — | — | — | + | — | — | 15.0 | 11,600 | —10 | — | — |
| 7 | 30 | 12 | — | + | — | — | + | — | + | 12.0 | 8,900 | + 2 | — | — |
| 8 | 24 | 5 | — | — | — | — | — | + | + | 10.2 | 8,000 | — 2 | — | — |
| 9 | 18 | ? | — | — | — | — | — | — | — | — | — | — 1 | — | — |
| 10 | 24 | 11 | — | + | — | — | + | — | + | 11.0 | 10,700 | + 7 | — | — |
| 11 | 30 | 2 | — | — | — | — | — | + | + | 11.6 | 6,500 | — 1 | — | — |
| 12 | 17 | 5 | — | — | — | + | + | — | + | 12.3 | — | + 2 | + | — |
| 13 | 31 | 12 | — | — | — | — | — | + | — | 14.4 | 6,000 | — | — | — |

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Examination of the patient revealed a process localized on the face, such as the previous patients had presented, with the addition of large pitted scars. The

absence of comedos was a conspicuous feature. The general examination revealed septic tonsils, grade 2 (on a basis of 1 to 4), and a small but not infantile uterus. Studies of the blood disclosed a hemoglobin content of 11.9 Gm per hundred cubic centimeters of whole blood, the erythrocyte and leukocyte counts were normal.

The basal metabolic rate was -7 per cent. Results of intradermal testing with old tuberculin were negative. Results of roentgenologic examinations of the teeth and thorax were also negative. Cultures taken from the abscesses and pustules on two occasions exhibited no growth in forty-eight hours.

We frequently heard from the patient until July 1937, each letter stating that she felt well and that there had been no recurrence of the pyoderma. She said that the scars were gradually becoming less noticeable.

CASE 4—A single white woman 21 years old came to the clinic in July 1937, complaining of an intense pustular eruption of the face which had begun four weeks previously. The patient's family history was essentially not pertinent to her condition. She had always considered herself to be in excellent health. Her menstrual periods had begun at the age of 12 and had always been normal, except that the three menses just prior to her coming to the clinic had been less in amount and had lasted only three days instead of the usual five.

Six weeks prior to her admission to the clinic and two weeks prior to the onset of the condition, she had been vaccinated against smallpox. There was no history of previous *acne vulgaris*. The onset of her present condition had started with what she described as a severe "acne" of the chin, which in two weeks had spread to involve the right cheek.

Examination disclosed the patient's chin and cheek to be studded with deep, indurated abscesses and superficial pustules, some of which were connected by undermining channels. The whole region was edematous and presented a boggy appearance. On incision of the abscesses, a thick greenish yellow pus was evacuated. Results of her general physical examination were essentially negative except for dermatophytosis of the feet.

The hemoglobin content was reported as 9.1 Gm per hundred cubic centimeters of whole blood. Results of roentgenologic examination of the thorax were negative. Roentgenologic examination of the teeth revealed one periapically infected tooth. The basal metabolic rate was 0. A culture of the material from the abscesses and pustules showed no growth in forty-eight hours. In spite of persistent therapeutic efforts, the patient's entire face soon became involved. Typhoid vaccine was administered intravenously, after which procedure she rapidly improved. At the time this paper was written (1939) the patient had no further difficulty with her skin.

ETIOLOGIC CONSIDERATIONS

We have not been able to determine the causative factor of pyoderma faciale. Although tuberculosis is prominent among the considerations in eruptions of this type, we have not been able to establish a tuberculous conception of this disease. Many conditions belonging to the pyodermas and granulomas often have a histologic picture consisting of epithelioid cells, lymphocytes and giant cells (usually of the foreign body type), and may not have a definite tubercle formation. Such a formation is, however, only presumptive evidence that the process is of tuberculous origin, unless *Mycobacterium tuberculosis* actually is demonstrated.

Tuberculosis in the family background was reported by only 2 of our 13 patients, and the condition in 1 patient was probably tuberculous arthritis. Results of roentgenologic examinations of the thorax in 12 of the 13 patients were negative for tuberculosis. Intradermal testing with purified protein derivative of tuberculin produced negative reactions in 4 of 5 patients.

Van Studdiford⁷ recently reported on the value of tuberculin, both human and bovine types, in the treatment of certain types of acneform eruptions. He apportioned the acnes he had observed into three classes. According to the description and the 1 photograph accompanying his report, the condition encountered in his third class somewhat resembles that in our series of cases.

None of our patients was treated with bovine or human tuberculin. In specimens taken from 2 of our patients for whom biopsies were performed, there was no histologic evidence of tuberculosis, although in 1 case studied elsewhere the specimen was diagnosed histologically as tuberculous.

Guinea pigs inoculated with aspirated material obtained from 1 of the patients exhibited no evidence of having tuberculosis when they were killed seven and one-half weeks after inoculation. Cultures of the aspirated pustular material of 6 patients gave negative results bacteriologically, results of culture of the blood were negative for 1 patient.

Foci of infection, found in the teeth or tonsils or in both, were present in 6 of our 13 patients. In our series the disease had no apparent relationship to the social status or occupation of the patient or to the type of body framework. A history of previous acne and evidence of its previous existence characterized 6 of our patients, and seborrhea of the scalp afflicted 7 patients. None of the patients had a history of ingestion of iodides or bromides.

Premenstrual or menstrual exacerbations, which are so prominent in the conditions of patients who have acne vulgaris, affected only 4 of the 13 patients. In 1 instance the duration of the menses decreased from a normal period of five days to two or three days, however, the pyoderma of this patient did not become worse before or during menstruation.

Determination of values for estrogenic and gonadotropic substances gave no clue in 4 instances in which measurements were made. The basal metabolic rate produced no definite leads, it usually was within the lower half of the limit considered normal. It is interesting to note that a moderate to mild degree of anemia was noted in 9 patients. Only 3 patients did not have anemia.

⁷ Van Studdiford, M. T. Diagnostic and Therapeutic Use of Tuberculin in Certain Acneform Eruptions, *Arch. Dermat. & Syph.* **38**:737 (Nov.) 1938.

The significance of this observation in our estimation is that pyoderma affects principally persons whose general physical condition is deficient and who present a field in which the causative agent, whatever it is, can achieve success. The fact that the disease in our series occurred among young women and the fact that we have observed no analogous conditions among men are important, although their significance is not known. Equally important is the site of occurrence of the pyoderma, the lesions being sharply limited to the face.



FIG 4 (case 13)—Section showing the infiltrate lying deep in the cutis and composed of polymorphonuclear leukocytes, lymphocytes and epithelioid cells. Hematoxylin and eosin stain, $\times 80$.

HISTOPATHOLOGIC CONSIDERATIONS

The pathologic change noted in two biopsy specimens, one from an early lesion and the other from a late lesion, was an infiltrate composed of polymorphonuclear leukocytes and lymphocytes deep in the cutis (fig 4), situated perifollicularly and about the sebaceous glands. Early necrosis of the perifollicular connective tissue was noted, it gradually extended peripherally and centrally to cause destruction of the hair follicle and its accompanying sebaceous gland. The more superficial

coil glands also were destroyed. The disease process developed until isolated abscesses became confluent and merged into one large abscess.

In one section obtained for biopsy, several of the hair follicles were markedly dilated and contained keratinized material. However, no definite comedos were seen. There was complete loss of connective and elastic tissue deep in the cutis at the regions of necrosis. The changes in the blood vessels consisted of dilatation of the capillaries. In one section, a portion composed of epithelioid cells, leukocytes and a giant cell of the foreign body type was observed. We were unable to demonstrate acid-fast bacilli by means of special stains.

COURSE AND TREATMENT

The course of pyoderma faciale is characterized by periods of rapid spread. In 4 instances the spread was attributable to premenstrual or menstrual exacerbations. In other cases no explanation for the spread was found. One patient had a recurrence, the first attack had occurred four years previously but had subsided under therapy in six months' time and had recurred four weeks prior to her admission to the Mayo Clinic.

The duration of the disease up to the time of the patient's admission to the clinic varied from one month to one year. From these data it seemed apparent that the maximal involvement was reached from within a few weeks up to three months after the onset of the disease (in 1 instance the disease progressed for six months), and after this the process either remained stationary or slowly resolved.

The survey of these cases indicates that in an occasional patient the disease tends to undergo spontaneous involution. Whether this involution is caused by previous treatment or is due to a natural course of events is unknown.

It is our impression that the eventual outcome of the disease in the majority of cases is disappearance within approximately a year.

Two types of treatment were used in the care of the patients. The first consisted of local measures, which in general were those used in the care of acne vulgaris. Sulfur lotions, wet dressings and the stronger peeling ointments were employed as seemed indicated, the use of these was combined with judicious treatment by incision and drainage of the pustules and abscesses. The majority of patients (8 of the 13) received both filtered and unfiltered roentgen ray therapy. Ultraviolet irradiation was used for 4 patients, both locally to the face and generally to the trunk.

The second type of therapy was directed toward the systemic status of each patient. We believe that with the use of the local measures, including incision and drainage, in conjunction with the administration

of thyroid and ovarian extracts the results were definitely better than they would have been if these medicaments had not been used. With patients in whom the pyoderma was progressing in spite of local treatment, attention to the general condition was essential in bringing about regression of the disease.

It is interesting to note here that the patients who received roentgen ray therapy fared no better than the 5 patients who did not. From this it seems evident that there is no definite benefit to be gained from the employment of roentgen rays in the treatment of this condition.

We demonstrated to our own satisfaction that hospitalization materially hastened the arrest of this disease. Rest in bed, daily dressings, and a forced diet of a high caloric and high vitamin content in conjunction with the use of vitamin A, B and D supplements materially shortened the course of the disease.

Phenol and alcohol peeling therapy was used with benefit for the scarring, which was often keloidal. Occasionally, radium was used for the treatment of the more pronounced keloidal scars. With this procedure the average period of treatment lasted from six to eight weeks.

The pyoderma of 2 patients progressed in spite of intensive therapeutic efforts, and it was not until foreign protein therapy in the form of typhoid vaccine was administered intravenously that we noted any improvement.

The involution with this varied therapeutic procedure, together with our inability to demonstrate the presence of tuberculosis in the cutaneous lesions or elsewhere with any degree of regularity, has led us to believe that pyoderma faciale is primarily an infectious process.

SUMMARY AND CONCLUSIONS

A unique form of facial pyoderma which afflicts young women is described.

This condition, although a disease of the sebaceous structures, is characterized by an infection of the sebaceous glands and perifollicular tissues, it is marked by an absence of comedos, a rapid onset and a fulminating course, strict localization to the face and absence of acne-form lesions on the chest and back.

The disease is etiologically obscure. We were unable to find evidence to support the conclusion that the condition is tuberculous.

Treatment tends to shorten the duration of an occasionally self-limited disease process. Best results therapeutically are obtained by a high vitamin diet with administration of vitamin supplements, rest in a hospital, ultraviolet ray therapy, local surgical treatment, administration of thyroid and ovarian extracts and, on occasion, intravenous administration of typhoid vaccine.

PINTA IN CUBA

SPECIAL CLINICAL FEATURES OF THE CUBAN CASES AND
DISCOVERY OF A SPIROCHETE IN ACTIVE LESIONS
AND IN THE LYMPH GLANDS

BRAULIO SÁENZ, M D

IN COLLABORATION WITH

JUAN GRAU TRIANA, M D

AND

J ALFONSO ARMENTEROS, M D

HABANA, CUBA

Although pinta is common in Mexico and Colombia, countries where it reaches endemic proportions, this peculiar dyschromic condition has likewise been observed for many years, but in a smaller proportion, in the tropical regions of the New World—Venezuela, Brazil, Peru, Central America and the West Indies. The condition is called *boussavolle* in Haiti, *guassarole* in the Dominican Republic and *piquete* in Guadeloupe.

In Cuba, the largest and most populous island in the Caribbean Sea, with a high mean temperature, high humidity and heavy rainfall, all conditions which are considered to be favorable for the existence of pinta, there were no cases reported before the year 1929. I have reached this conclusion after a thorough and careful study of the Cuban medical literature and would add that I have been unable to find any description under another name of a condition which might correspond to the disease in question.

The story of pinta has developed in three stages. The first period extended from 1921 to 1929, during which time the condition was considered to be a special type of late keratotic syphiloderma of the palms and soles. The second commenced in 1929, when this condition was presumably identified as *caraté*. The third began on Aug. 3, 1938, with the discovery of the spirochete which causes the condition and with the confirmation of the hypothesis previously formed as to the spirochetic nature of the disease.

Between 1921 and 1929 a series of cases was studied in which the patients presented symmetric keratoses of the palms and soles with subsequent extension to the dorsa and in some to the arms and legs. The condition was characterized by slate blue achromic changes of the flexor

Read at the Sixty-Second Meeting of the American Dermatological Association, Inc., Monte-Bello, Quebec, Canada, June 1, 1939

aspects of the wrists In the final stages there was slight atrophy Evolution was slow and extended in some cases over twenty years There was no history of syphilis, but the Wassermann reaction was strongly positive in all patients, and the lesions yielded to antisyphilitic treatment

These facts and the infiltrated and elevated borders, at times polycyclic, led to the consideration of the process as a late syphiloderm *en nappe* Nevertheless histopathologic studies did not substantiate the theory of syphilis

The first patient observed consulted me in December 1921 in the dermatologic department of the Mercedes Hospital for a condition that had been treated in other departments for over two years without result, it had been considered as *tinea albicans* Nieuwenhuis by some and as an undetermined mycotic infection by others In consequence, the lesions had been treated with iodine and salves

Direct examinations of the scrapings and cultures were made, the results of both being negative for fungi This result could be presumed from the clinical features, which did not correspond to those observed in fungous diseases

Palmar psoriasis, dry squamous eczema and other keratoses could be eliminated

I was much surprised at not finding in any of the 7 cases studied in the first period any histologic substantiation of syphilis, and I thought the condition might be due to an advanced stage of terminal atrophy which could result from syphilis as well as from any other chronic inflammatory process The shortest duration of the lesions in these cases was ten years, and in some the course extended to twenty years

In June 1928 Pardo-Castello, discussing a case presented at the clinical meeting of the Cuban Dermatological Society, made the following statement ¹ "At the last meeting of the American Dermatological Association, Dr Howard Fox presented photographs of Colombian cases of carate, which struck me as being cases of exactly the same condition as that in the case presented"

A case of "late keratotic and atrophic syphiloderma of the palms and soles" was presented at the clinical meeting of the Cuban Society of Dermatology in January 1929 ² Dr Howard Fox was invited to discuss the case and stated "In my recent trip to Colombia for the study of carate, I have observed that the dyschromic changes of the wrists as seen in this patient correspond to similar changes observed in carate, although the rest of the picture is different" He expressed

1 Pardo-Castello, V, in discussion on Grau, Ferrer and Pelaez A Case for Diagnosis, Arch Dermat & Syph 19 155 (Jan) 1929

2 Bol Soc cubana de dermat y sif 1 63. 1929

the opinion that keratoses never affected the palms and the soles of patients with pinta

He eliminated late syphilis from the possible diagnosis because of the superficial infiltration and because the condition was bilaterally situated on the hands and feet

It is thus plain that vitiligoid changes of the wrists formed the only feature relating the condition in the first of these cases to carate or pinta

At the clinical meeting of the American Dermatological Association in Habana on May 4, 1932, 4 new cases were presented³ Once again Dr Fox cooperated in an attempt to identify the condition and stated "I naturally hesitate to make a diagnosis of a disease heretofore unrecog-

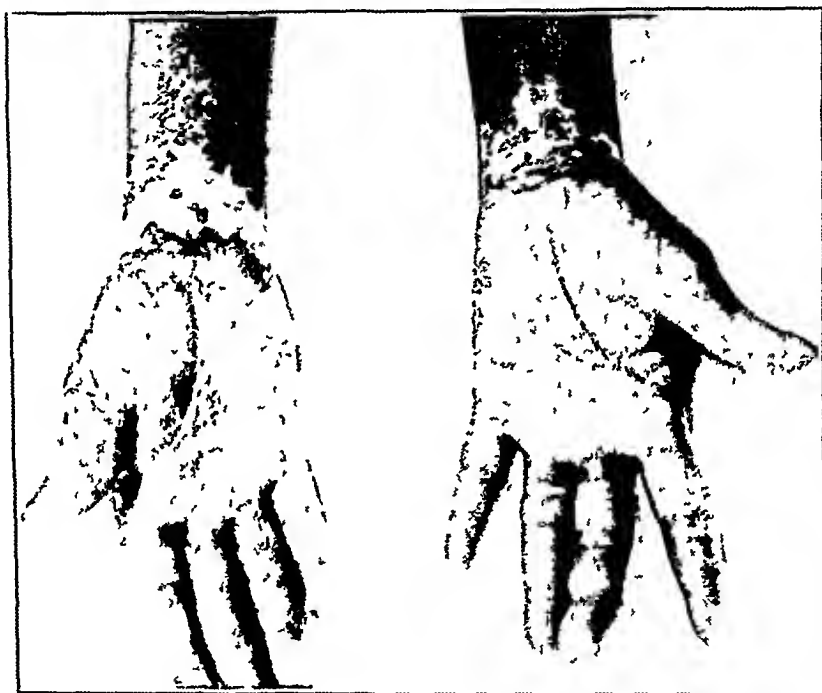


Fig 1—Characteristic V-shaped areas of complete depigmentation on the front of the wrists

nized in Cuba, but I think the supposition that this condition is pinta is correct "

In another communication, read by Dr Fox⁴ before the Eighth International Congress of Dermatology, he expressed his point of view that

3 Pelaez, A Syphilitic Leukoderma and Keratosis ? Pinta ? Arch Dermat & Syph 26 920 (Nov) 1932 Pardo-Castello, V, and Ibarra, R Syphilitic Leukoderma and Keratosis ? Pinta ? *ibid* 26 921 (Nov) 1932 Pardo-Castello, V Syphilitic Leukoderma (Symmetrical) and Keratosis ? Pinta ? *ibid* 26 921 (Nov) 1932, Syphilitic Leukoderma with Atrophy ? Pinta ? *ibid* 26 922 (Nov) 1932

4 Fox, H Mal del Pinto as Observed in Mexico Its Relation to Carate, read before the Eighth International Dermatological Congress, Copenhagen, 1930

pinta was due to some spirochete, thus sharing the opinion given by Dr S Gonzalez Heriejon in 1927

In this regard it is impossible to overlook the valuable contribution that Walter Menk made in 1926, in which he showed that the Wassermann reaction⁵ was positive in 74.5 per cent of the cases of pinta. Thus he proved the error of Chavarria and Shipley,⁶ who stated that "the Wassermann test in cases of *carate* is generally negative." Menk stated the belief that the development of *carate* was in some way related to an old spirochetosis and that at least there was an association of etiologic factors.

That the Wassermann reaction was positive in Cuban patients with keratoses on the palms and soles and with vitiligoid changes of the wrists was known to me from the time the first patient was observed, in 1921, although the identity of the disease with pinta could not be established.

Such a possibility was not determined, in my opinion, until 1935. Keratoses on the palms and soles were a constant feature of Cuban pinta, though they were never reported in the classic descriptions of the disease. I pointed out this fact in an address read before the Academy of Medicine in Mexico, D F, Mexico, on Oct 19, 1938, and in a paper⁷ about the pinta problem in Cuba.

Since 1935 routine examination of the cardiovascular system, spinal fluid and coexisting conditions has been carried on in a further series of cases.⁸ Microscopic sections, stained according to Levaditi's, Warthin's and other technics, failed to demonstrate the presence of the supposed causative spirochete. Similar negative results have been reported by other investigators.

In my opinion, these facts were responsible for the failure the patients had received previous therapy, the material for biopsy had been taken from permanent leukodermic lesions or from patients in whom the disease had spontaneously regressed, or an improper technic had been chosen.

These routine examinations were performed according to my instructions by my collaborators, in the serologic, bacteriologic and histologic departments of my service. The study of the cardiovascular system

5 Menk, W. *Carate in Colombia*, in Fifteenth Annual Report of the Medical Department of United Fruit Company, New York, United Fruit Company, 1926, p 123.

6 Chavarria, A P, and Shipley, P G. Beitrag zur Kenntnis der "Carate"-Arten des tropischen Amerika, Arch f Schiffs- u Tropen-Hyg 29 605 (Oct 15) 1925.

7 Saenz, B, and Grau Triana, J. Estado actual del problema de la pinta en Cuba, Rev de med y cir Habana 44 1 (Jan 31) 1939.

8 Grau Triana, J. Contribucion al estudio de la pinta o carate en Cuba, Arch de med int 3 125 (March-April) 1937.

and the roentgenograms were made in the corresponding departments of the Mercedes Hospital, Habana

The number of patients thus examined amounted to 30. Report was made only of those with cardioaortic lesions, changes in the spinal fluid or coexisting conditions. None of them had a history of syphilis, and all presented keratoses on the palms and soles, dyschromic changes of the skin and positive serologic reactions.

SPECIAL CLINICAL FEATURES OF CUBAN PINTA

The evaluation of the data obtained from patients, corroborated by careful observation of 50 patients I have examined, permits the statement that in Cuba *pinta* in its primary stage is limited exclusively to the palms and soles, with subsequent extension to the backs of the hands and in some cases to the arms and legs. One of the patients exhibited pigmentary disturbances on the face, and another showed similar disturbances on the abdomen and thighs,⁹ but these were the sole exceptions. The evolution of the disease is extremely chronic, in some cases extending over twenty years.

Keratosis of the palms and soles constitutes also an outstanding characteristic of the Cuban cases. Its first manifestation consists of rounded or irregularly outlined hyperpigmented spots which enlarge peripherally, becoming at the same time more numerous. Newly formed areas also turn into keratoses, which extend over the whole of the palms and soles. The skin appears dry and yellowish and becomes squamous at times when involvement is severe. Very rarely it also shows the sago-like hardened claviform keratoses. Fissures may develop, interfering with manual work and with walking when located in the furrows or in the joints.

In a more advanced stage the pigment is destroyed, with resulting production of permanent achromic areas. It must be emphasized that among over 100 patients I have examined in Mexico, rudimentary keratosis of the central part of the hands has been observed in 2. According to the statement of physicians with wide experience on the subject, keratoses are not observed in patients with *pinta* in Mexico, and dyschromic changes of the palms are also rare.¹⁰

In a small number of cases the lesions extended to the arms and legs, the number of plaques usually being limited to one or two. Keratoses never affected the backs of the hands or feet, although encroaching on the borders was frequently seen.

The pigmentary changes in the wrists are always of the slate blue variety, with areas of normal pigmented skin persisting in the leuko-

⁹ Pardo-Castelló, V. *Pinta o carate en Cuba*, Rev. de parasitol., clin. y lab. 2:667, 1936.

¹⁰ Gonzalez Herrejon, S. *El mal del pinto*, Leverkusen, 1938.

dermic patches. The border of the lesions is frequently raised slightly and more or less infiltrated, sometimes presenting the shape of a V and sharply limited or ill defined.

This limitation of lesions to the aforementioned regions contrasts with the common extension to the face, trunk, abdomen, arms, thighs, and entire body described in the classic articles on the subject.

Achromic plaques may present different aspects according to the degree of atrophy which is responsible for the pigmentary changes, it may be superficial when affecting extensive areas or deeper and pitted, as if produced by a pinpoint, when in limited areas. In the former

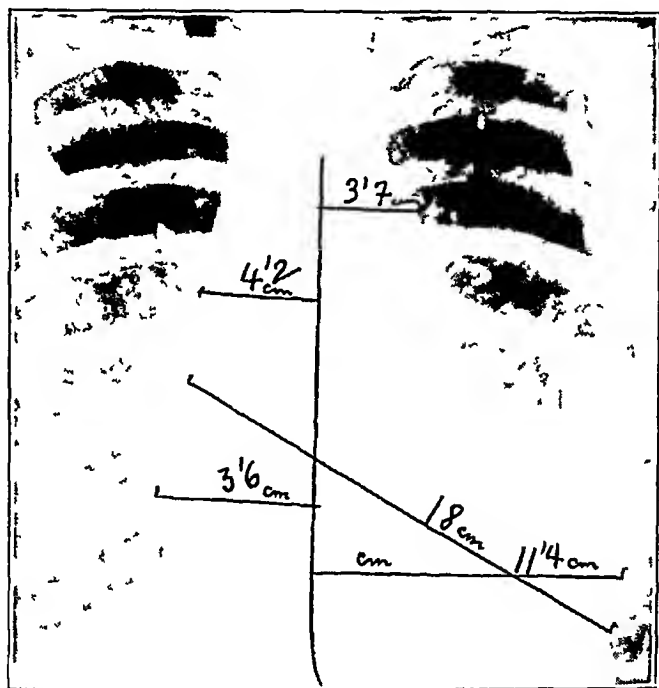


Fig 2—Roentgenogram showing aortitis in a case of pinta

case the skin appears smooth and shiny as in senile atrophy, in the latter alternating atrophic points, surrounded by normal skin, render the surface rough and uneven, so as to be comparable to that of fine sandpaper or of shagreen leather. Diffuse achromia is to be seen in the arms and legs, never constituting the initial manifestation of the disease and always following the keratoses on the palms and soles or the vitiligoid changes of the wrists.

The color of the pigmentary disturbances is also characteristic. It is always slate blue. I have never seen in Cuban patients yellow, erythematous or violet varieties, many of which I have seen among the Mexican patients.

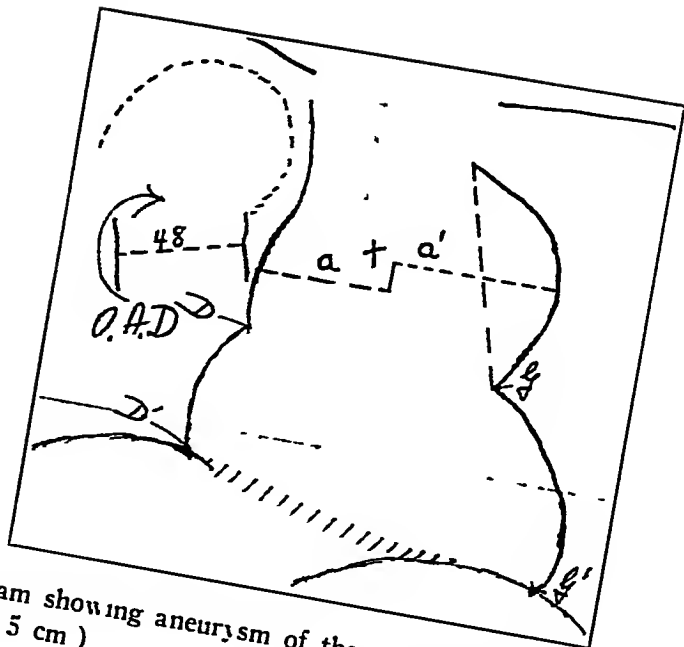


Fig 3—Diagram showing aneurysm of the ascending aorta $a + a' = 11$ cm
(normal = $4.5 \pm .5$ cm)



Fig 4—Areas of complete depigmentation of the hands and feet and a juxta-articular nodule in a patient with incomplete crossed variety of pinta

Data on Some of the Cases Studied

| Case | Race | Age | Sex | Occupation | Birthplace | Years of Duration of Disease | Reaction to Meinkne Test | Reactions to Spinif Fluid | Cardiovascular | Coexisting Conditions |
|------|---------|-----|-----|------------------------|---------------|------------------------------|--------------------------|--|---|----------------------------|
| 8 | Negro | 47 | ♀ | Washwoman | Matanzas | 17 | ++++ | Normal | Aortitis | |
| 10 | Negro | 56 | ♀ | Cook | Santa Clara | 16 | ++++ | Normal | Aortitis ven
tricular hyper-
trophy | |
| 12 | Mexican | 55 | ♀ | Washwoman | Pinar del Rio | 21 | ++++ | | | Juxta articular
nodules |
| 13 | White | 53 | ♂ | School teacher | Matanzas | 11 | ++++ | Normal | Aortitis, ven
tricular hyper
trophy | Leukoplakia |
| 15 | Negro | 67 | ♀ | Washwoman | Santa Clara | 20 | ++++ | Normal | Aortitis | |
| 17 | Mexican | 50 | ♂ | Peddler | Habana | 18 | ++++ | Increased glob
ulin, Meinkne
test, ++ syphilitic
colloidal gold curve | Aortic aneurysm | |
| 20 | Negro | 56 | ♀ | Homework | Habana | 9 | ++++ | Normal | Systolic murmur
point | |
| 21 | Mexican | 39 | ♂ | Policeman | Habana | 11 | ++++ | Normal | Reinforcement
of second tone | |
| 24 | Mexican | 16 | ♂ | Student | Habana | 4 | ++++ | Normal | | Epilepsy |
| 25 | Mexican | 51 | ♂ | Mail carrier | Habana | 14 | ++++ | Normal | | Leukoplakia |
| 27 | Negro | 44 | ♀ | Washwoman | Matanzas | 12 | Repeated — | Increased glob
ulin, Kahn test,
++, Meinkne
test, ++ syphilitic
colloidal gold curve | | |
| 29 | Negro | 78 | ♂ | Warehouse
attendant | Habana | 26 | ++++ | | | Leukoplakia
epithelioma |
| 30 | Negro | 40 | ♂ | Truck driver | Matanzas | 12 | ++++ | Meinkne test,
+++ syphilitic
colloidal gold curve | | |

In some of the cases there were hard, multiple, noninflammatory, medium-sized, superficial enlargements of the lymph nodes. Also in a few, changes of the nails, consisting of thickening with partial or total black pigmentation, were seen.

It must be pointed out that the serologic reaction was persistently positive in all cases, even when antisyphilitic treatment was given for long periods, although the lesions yielded rapidly to the treatment.

Of 30 cases that were studied, cardioaortic lesions, such as aortitis, aneurysm, enlargement of the diameters of the heart and valvular conditions, were demonstrated in 23.3 per cent. Similar findings have been reported in Colombia by Thonnard-Neumann and Camacho Moya,¹¹ the incidence in their cases being 80 per cent.

Changes in the spinal fluid were observed in 10 per cent of the cases. These changes were increased globulin, a syphilitic colloidal gold curve and a positive Meinicke reaction. In 1 case repeated tests gave negative results in the blood and positive results in the spinal fluid, which also showed increased globulin and a syphilitic colloidal gold curve.

It is interesting to note that in 1 case there was a juxta-articular nodule of the lower part of the right leg. This condition occurs also in syphilis and in frambesia.

COMMENT

A review of the literature on keratosis in order to verify the identity of the peculiar variety just described permits the elimination of the cases reported by Castellani and Chalmers¹² as well as those mentioned by Howard.¹³

However, I consider of the utmost importance the paper published by Gutiérrez,¹⁴ "Keratosis Palmaris et Plantaris Due to Frambesia." This reported on 431 cases of keratosis observed in 658 patients with active frambesia lesions. Four cases were studied in detail and illustrated with excellent photographs.

The description of the lesions and the illustrations are similar if not identical to the corresponding features of keratosis observed in Cuban pinta. Also the histologic pictures correspond to those in our cases. However, pinta has not been reported in the Philippine Islands, as far as I know, but has always been considered a disease existing exclusively

11 Thonnard-Neumann and Camacho Moya. Is Carate a Dermatomycosis? in Nineteenth Annual Report of the Medical Department of United Fruit Company, New York, United Fruit Company, 1930, pp. 101-106.

12 Castellani, A., and Chalmers, A. J. Manual of Tropical Medicine, ed. 3, New York, William Wood & Company, 1919, p. 1550.

13 Howard, R. The Importance of Tertiary Yaws, *J. Trop. Med.* 18:25, 1915.

14 Gutiérrez, P. D. Keratosis Palmaris et Plantaris Due to Frambesia, *Arch. Dermat. & Syph.* 8:382 (Sept.) 1923.

in the tropical countries of the American continent. Climatic conditions favorable to the existence of pinta are present in the Philippines, and so, theoretically, the disease might occur there.

Cases of frambesia with keratosis similar to that in pinta have also been reported by Cordes¹⁵ who, in 78 cases of frambesia observed in the oriental province of Cuba, encountered in 4 of them, all of whom were old male Haitians who came to Cuba in 1918 as cane cutters, atrophic changes of the palms and soles, with irregular areas of depigmentation, resulting in a marmoriform appearance.

In none of the 50 cases studied in the preparation of the present paper was there any detail which would permit one to suspect a previous history of frambesia. The patients were all Cubans, none came from the oriental province, and none had the morbid changes in the periosteum or in the bones so characteristically common in the late stages of frambesia.



Fig. 5—Spirochetes obtained from active lesions after abrasion of the epidermis (stained by the Fontana method)

HISTOLOGIC PICTURE

A consideration of the histologic picture of pinta will be omitted, as no new findings could be added to the last contribution on the subject. Instead the histologic picture of keratosis is reported, because of its constant and outstanding importance.

The lesions are confined to the epidermis and corium, the most important changes are in the horny layer and are manifested by pronounced hyperkeratosis. The thickness of the stratum corneum is increased, sometimes to as much as fifteen times the normal dimension. The cells become so completely cornified that they form dense, hard, homogeneous horny masses, so that it is difficult to determine the outline of the separate cells. The granular layer is in places slightly increased.

15 Cordes, W. Syphilis and Frambesia Among Haitian Laborers in Cuba, in Fifteenth Annual Report of the Medical Department of United Fruit Company, New York, United Fruit Company, 1926, p. 156.

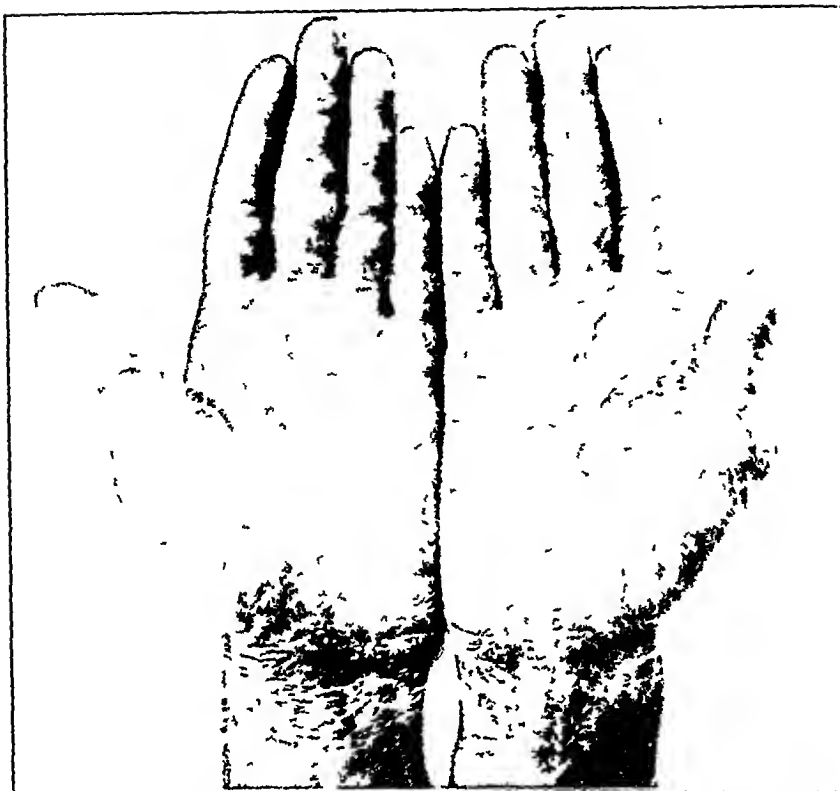


Fig 6—Keratosis and depigmentation of the palms and wrists



Fig 7—Infiltrated lesions of the heel and the dorsum of the foot

and in others five times thicker than normal, and the outline is irregular. The stratum lucidum is clearly outlined.

Acanthosis is more pronounced in the early stage of the keratotic condition than in late periods. No infiltration of the rete is observable.

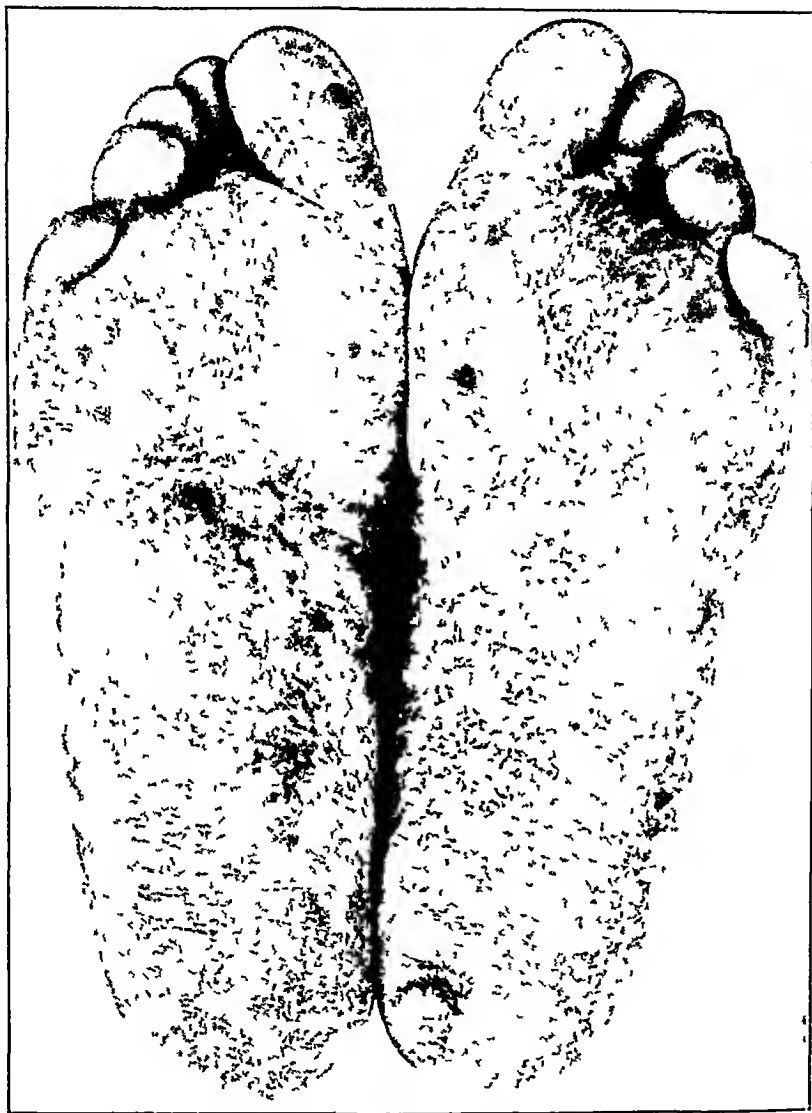


Fig. 8—Keratosis and depigmentation on the soles

In places the papillae are flattened, and in others, hypertrophied. Slight edema of the papillary and subpapillary layers is observed.

Cell infiltration, composed mostly of plasma cells and to a less extent of round cells, is limited to the papillary layer and located in the vicinity of the blood vessels.

DISCOVERY OF THE SPIROCHETE

On Aug 3, 1938, the causative spirochete was demonstrated for the first time, in the serum obtained after abrading the epidermis of dyschromic lesions of the wrists and ankles

REPORT OF A CASE

The patient was a Negro janitor aged 60, born in Habana. His past history was unimportant. He stated that the disease had commenced ten years previously.

The lesions were limited to the hands and feet and consisted of symmetric keratoses on the palms and soles, more pronounced on the latter, where they were

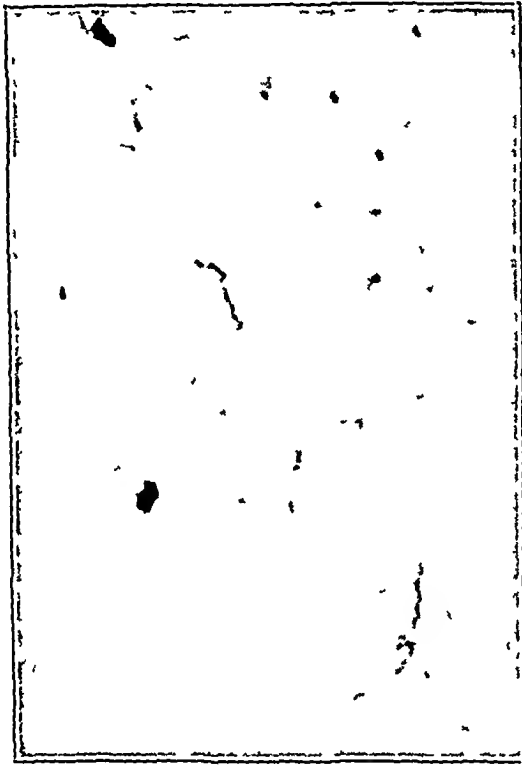


Fig 9—Spirochetes (stained by the Levaditi method)

massive and became squamous and fissured. An encroaching on the border on the hands and feet was observed. The skin was deeply infiltrated and slate colored. Superficial atrophy was evident on the backs of the hands, but there was no discoloration. The palms were studded with irregularly shaped areas of hyperpigmentation, surrounded by less numerous, smaller depigmented spots. Some of the toe nails were thickened and coarse with blackish pigmentation. The patient also presented multiple hard, medium-sized, noninflammatory, superficial enlargements of the lymph nodes in the inguinal region, epitrochlea and biceps muscle.

The Wassermann and Meinicke reactions were strongly positive. The spinal fluid and the cardiovascular system were normal. Dark field examination of serum obtained after abrading the epidermis in the dyschromic lesions of the wrists and the lateral side of the foot demonstrated abundant spirochetes which were morphologically identical with *Spirochaeta pallida* and *Spirochaeta pertenuis*. On

August 5 this discovery was reported to the Cuban Society of Dermatology and Syphilology.¹⁶ Two days later similar spirochetes were found in material aspirated from the lymph nodes with a syringe.

These observations were confirmed a week later at the Calixto Garcia Hospital, in the service of Dr. Pardo-Castello.

Biopsy specimens were obtained from the infiltrated lesions on the dorsa of the feet, and the organisms were seen in the prickle cells.

Staining of tissues for spirochetes gave positive results in only 2 cases and failures in 30. Positive results were obtained in deeply infiltrated lesions, which are rarely observed. Even in cases in which spirochetes were detected by means of dark field examination results were negative in the tissues, although material for biopsy had been taken in places where spirochetes had been previously demonstrated.

The presence of spirochetes in active pinta lesions was confirmed by the Mexican Commission for pinta on Oct. 17, 1938, in 98 of 100 cases in Iguala, Guerrero.

My co-workers and I found the spirochetes in 31 of 34 cases in the same locality on October 22, only five days later. Of 6 new cases in which examinations were made recently in Habana, spirochetes were demonstrated in all.

In a personal communication dated Feb. 2, 1939, Dr. David Iriarte, from Caracas, Venezuela, stated that spirochetes had been demonstrated in persons with carate, and he reported this finding to the Academy of Medicine of that country.

Brumpt¹⁷ reported on March 11, 1939 the discovery of *Treponema carateum* to the Société de biologie of Paris.

SUMMARY AND CONCLUSIONS

Future descriptions of pinta should include the peculiar features of the Cuban cases, such as keratoses on the palms and soles, limitation of the process to the hands and feet with extension to the arms and legs only in a small number of cases and pigmentary changes uniformly corresponding to the slate blue variety.

It is interesting that the keratoses present a striking similarity to those reported as a late manifestation of frambesia and to a lesser extent to certain syphilodermas. Differential diagnosis, made on purely clinical

16 Saenz, B., Grau Triana, J., and Alfonso, J. Demonstración de un *Treponema* en el borde activo de un caso de pinta de las manos y pies y en la linfa de ganglios superficiales. Reporte preliminar, *Arch. de med. int.* **4**: 112 (Jan.-Feb.) 1938.

17 Brumpt, E. Un nouveau treponème parasite de l'homme *Treponème carateum*, agent des carates ou "mal del pinto," *Compt. rend. Soc. de biol.* **130**: 942 1939.

grounds and from laboratory observations of keratoses corresponding to the first group, is almost impossible. The rest of the clinical picture and a history of the case are always of the utmost importance.

Cardiovascular lesions were present in 23.3 per cent of the cases and changes in the spinal fluid in 10 per cent. Such observations should be interpreted not as a coincidence but as being in direct relation to the disease. Juxta-articular nodules are observed in pinta as well as in frambesia and syphilis.

That pinta is an endogenous, specific and chronic disease is proved by serologic changes, enlargement of the lymph nodes and alterations of the cardiovascular system and spinal fluid. Only atrophy and the dyschromic changes represent the injury to the skin.

The supposed causative spirochete was discovered in the patient examined on Aug. 3, 1938, and this finding was conclusively confirmed by further investigations. The technic is simple: abrading of the epidermis and examination by means of the dark field illumination.

The relation of pinta to frambesia and to syphilis deserves careful consideration, and further research, especially as to the problem of cross immunity between these conditions, is necessary.

These questions cannot yet be solved because of the incomplete knowledge of the biologic factors.

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ABSTRACT OF DISCUSSION

DR HOWARD FOX, New York. Dr Sáenz has discussed two features of pinta of great importance: (1) the discovery of the causative organism and (2) the peculiar features of Cuban cases, which apparently differ from those in other parts of Latin America.

Dr Sáenz and his co-workers are to be congratulated on the discovery of the cause of the disease which is widespread in the American tropics. In the southern half of Mexico a careful census showed the presence of 270,000 cases. It is also estimated that there are as many or more in Colombia. Although the spirochete of pinta is morphologically identical with the spirochetes of syphilis and yaws, the symptoms of pinta are totally unlike those of the last-mentioned diseases.

I am delighted that this discovery refutes the theory of a fungous causation, which has held sway for forty years, since 1898, when Montoya y Flores tried to prove that various chromogenic fungi cause the different shades of color in pinta. For the past ten years I have been convinced that fungi play no part in causing pinta. The work of Menk in 1926, who found positive Wassermann reactions in nearly 70 per cent of cases of pinta, threw doubt on the theory of fungous origin. By better technic, the incidence of positive reactions was found to be nearly 100 per cent by the Mexican Pinta Commission. Furthermore, the fact that the disease (blue patches) responded to antisyphilitic treatment added strength to the suggestion of a spirochetal causation. Many clinical features also spoke against a fungous origin, notably, the rare cases of hemipinta, in which the disease appeared from head to foot on one side of the body.

Mention was made of my good fortune in being able to attend the meeting of the Cuban Dermatological Society on my return from Santa Marta. I felt sure that

the case presented by Dr Saenz was one of pinta because of the bluish and vitiligo patches and the positive serologic reaction. The hyperkeratotic lesions of the palms constitute a feature of pinta that was new to me and had not been mentioned by those who had written about pinta in other parts of Latin America. The general conception of the disease was that the cutaneous lesions consisted solely of pigmentary changes. The presence of juxta-articular nodes and positive serologic reactions of the spinal fluid have not been observed in other countries. Yaws has been discovered recently in Cuba, one of the characteristic manifestations of the disease being hyperkeratosis of the soles and less often of the palms. The presence of such lesions in pinta constitutes a new problem.

DR V PARDO-CASTELLO, Habana. One point I want to bring out is the reason why this condition was considered to be caused by a fungus for many years. Pinta was studied by specialists in tropical diseases, who examined the condition only from the general, or medical, point of view. The result was that it was known under the name of *pinta merle*. When the subject fell into the hands of competent dermatologists, Dr Gonzales Herrejon, of Mexico, studied the condition. Also, Dr Howard Fox can testify that Yucatan physicians considered it pinta. A variety of conditions were called pinta. These conditions of the skin were separated from pinta, and now the subject is limited to its right proportions. Many patients with pityriasis versicolor were considered to have pinta because they were seen by general physicians.

I corroborate Dr Saenz's findings in the spinal fluid. Among my own patients I have been able to find a number with positive reactions. There were increased globulin, a slight increase in the lymphocyte count and sometimes, but not always, a positive Kahn reaction. In the majority of cases, however, there were no clinical symptoms referable to the nervous system, and, as Dr Fox stated, the patients were never incapacitated as far as one could tell. As far as differentiation from syphilis is concerned, two points are of greatest importance. 1. Pinta is limited almost entirely to the colored race, only 2 cases have been observed in white persons. In Mexico, as well as in Colombia, all the patients reported on have been Indians. 2. It would be an unusual type of syphilis to be limited to the tropical belt of America. Pinta has never been reported in the United States or Europe or in the tropics of Asia and Africa. That is enough to rule out syphilis. Furthermore, the pathologic picture of the condition does not resemble that of syphilis.

Another point I want to bring out is the resemblance of pinta, as far as clinical appearance is concerned, to yaws in certain cases. Undoubtedly, the last stages of yaws, such as those which show pigmentary changes as well as hyperkeratotic conditions of the palms and soles, closely resemble pinta. Also, the outlines of some of the lesions of pinta are polycyclic, but that is nothing to be astonished about, because syphilis, yaws and pinta have certain features in common.

A piece of research was done in Mexico City recently. The finding of the spirochete in the lesion alone would not prove the causation of the disease. Naturally, since the organism is found in nearly every case, one must suspect that it is the etiologic agent. But recently the disease has been transmitted to man. A macular spot appears which spreads slowly and sometimes develops into a typical lesion of pinta. Material has been taken from the borderline of this lesion that is transmitted from man to man. The spirochete has also been recovered after a certain number of weeks. Therefore, it seems probable that the disease may be transmitted to man and the organism recovered from the infected person. I suspect, too, that in most cases of pinta one is dealing with a latent condition, and perhaps in the future it will be possible to demonstrate other manifestations, such as the recently acquired one—the infiltrative condition that may be the beginning stage

of the disease. In some cases it may be ten, fifteen and sometimes as many as twenty-five years before such manifestations are demonstrated.

DR BRAULIO SÁENZ, Habana. One good reason why the condition in the Cuban cases could not be identified with that in the Colombian and Mexican cases of *pinta* is that, as I have stated, keratoses of the palms and soles are constant in the Cuban cases. We have emphasized this characteristic in our paper and have stressed the fact that in over 100 cases in Mexico in which we made careful examinations keratoses were observed only twice and were rudimentary.

It appears that certain cardiovascular alterations detected in the course of *pinta* are in direct relation to this spirochetal disease and are not mere coincidences. These findings were reported first by Colombian investigators in the medical department of the United Fruit Company, at Santa Marta. The incidence in their cases was 80 per cent—three times higher than in our material. It is a well known fact that these alterations have not been observed in Mexico, and to my understanding the reason is obvious. Dr Fox, who has visited Iguala and Chilpancingo, *pinta* districts, knows that it is impossible in these localities to obtain the roentgen equipment indispensable for these investigations. When I visited these towns last October I had to transport from Mexico City over a mountainous road of over 300 miles the entire material and outfit necessary for demonstration of spirochetes. In Mexico City itself, cases of *pinta* are rare. All *pinta* infections are imported from distant states. The same difficulties obtain in the study of changes in the spinal fluid.

I cannot explain the exact relation of *pinta* to syphilis and frambesia. The spirochete of *pinta* is morphologically identical with the spirochetes of both of these diseases. Dr Aldo Castellani, during a recent visit to Habana, was shown the spirochete of *pinta* and confirmed my conclusions originally reported to the Cuban Dermatological Society on Aug. 3, 1938. Furthermore, these three conditions present sometimes similar clinical features, all show positive serologic changes and yield to antisyphilitic treatment. I believe at present that one cannot tell how far apart they are or how close they were in the early days of microbiology. An open field is left for further research along this line.

Regarding Dr Pardo-Castello's remarks, I must say that in Mexico some persons still consider that *empímes* is really *pinta*. He pointed out one subject which I could not read in my paper because of lack of time. Thus, I have studied in Cuba over 80 cases, and only 2 of the patients were white, the rest were Negroes and mulattos. This racial predisposition may have something to do with the special clinical features of Cuban *pinta* and at the same time may give a clue to the explanation of the differing features in the symptomatology. In this connection, I must mention the observations reported by Harper, in the Fiji Islands, where syphilis is unknown and frambesia is prevalent. He claims to have observed unquestionable cases of dementia paralytica and tabes dorsalis due to frambesia. In certain cases the clinical manifestations of *pinta*, syphilis and frambesia may be difficult to differentiate.

In my opinion, the spirochete is the causative organism of *pinta*. It is found in the prickle cells of the epidermis of dyschromic areas and not in places where the skin is normal or in normal persons. Moreover, the spirochetes always disappear after treatment.

Hansen's mycobacterium is accepted as the cause of leprosy in spite of the fact that no one has ever succeeded in experimentally inoculating animals or human beings. While I was in Mexico, experimental work on *pinta* was carried on in my dermatologic service in Habana. The cornea and testicles of rabbits were inoculated with fragments of tissues from persons with *pinta*, and keratitis and epididymitis similar to those obtained in experimental syphilis resulted.

RECKLINGHAUSEN'S DISEASE

ITS ELUSIVE MANIFESTATIONS AND INTERNAL RELATIONS

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In recent times, knowledge of the far flung relations of the syndrome originally described by von Recklinghausen¹ in 1882 has made phenomenal progress. Von Recklinghausen considered the process to be essentially a hypertrophy of the mature connective tissue of normal nerves. He recognized several varieties of the disease and later objected to the term neurofibromatosis, because it gives a misleading impression of the nature of the disease. Further objections to the name "generalized neurofibroma" were advanced, because it was felt that undue emphasis was being placed on but a single aspect of a complex syndrome. Such a syndrome should be designated by a term broad enough to include all its recognized manifestations, but at the present time there is no better name than Recklinghausen's disease.

The first descriptions of the gross anatomic lesions were made by Smith² in 1849. Fifteen years later Virchow³ published his researches on the origin of the growths. He stated the belief that they originated from the connective tissue elements of nerve fibers.

The purpose of this paper is to correlate the varied observations, to revise the original cutaneous classifications and to propose several new concepts of endocrine interrelation.

ETIOLOGY

The cause of Recklinghausen's disease is not known. However, a number of probable causative factors have been advanced by their various proponents.

1 von Recklinghausen, F. Ueber die multiplen Fibrome der Haut und ihre Beziehung zu den multiplen Neuomen, in Festschrift zur Feier des Funfundzwanzigjährigen Bestehens des pathologischen Instituts zu Berlin, Berlin, A. Hirschwald, 1882.

2 Smith, R. W. A Treatise on the Pathology, Diagnosis and Treatment of Neuroma, Dublin, Hodges & Smith, 1849.

3 Virchow, R. Die krankhaften Geschwulste. Dreissig Vorlesungen, gehalten wahrend der Wintersemestern 1862-1863 an der Universitat zu Berlin, Berlin, A. Hirschwald, 1863-1867.

Heredity—Several conclusive studies indicating the transmission of neurofibroma as a dominant genetic characteristic have been carried out. In 1915 Preiser and Davenport⁴ observed 115 siblings the 20 parents of whom had Recklinghausen's disease and noted that 43 per cent of them were similarly affected. On the other hand, Acuña and Bazán⁵ in 1924 described 8 cases in which they did not observe anything suggestive of the importance of heredity. Two of their patients had abnormalities of the spine, 3 had dysfunctions of the endocrine system and 2 had congenital syphilis. A more recent study by Gardner and Frazier⁶ (1930) was made of a family of 38 persons with deafness due to bilateral neurofibromas of the acoustic nerve. Apparently the larger series of cases suggest a definite hereditary influence.

Endocrine Glands and the Autonomic Nervous System—The Italian endocrinologist Pende⁷ presented a most suggestive theory as to the causation of Recklinghausen's disease. Pende expressed his opinion (with, to quote Muto,⁸ "many learned arguments") that the sympathetic nervous system and the glands of internal secretion constitute two physiologically and pathologically synergic systems, so that a morbid process localized in one system makes its effects felt in the other, he maintains that a whole series of conditions which have been included either under diseases of the nervous system or in the group of disorders of the glands of internal secretion should be combined into one group of endocrine-sympathetic dysfunctions. The common symptomatic picture would consist essentially of a more or less complex dystrophy (disturbances of metabolism and anomalies in tissue development), accompanied by symptoms due to a functional disturbance of one of the endocrine glands. Among such dystrophies he places scleroderma, painful lipomatosis (Dercum's) and neurofibromatosis. For the production of these conditions two factors are required: (1) a constitutional factor, represented by an abnormality of the endocrine-sympathetic system, which may be hereditary, intrauterine or extra-

4 Preiser, S. A., and Davenport, C. B. Multiple Neurofibromatosis and Its Inheritance, with Description of a Case, *Am J M Sc* **156**:507-540 (Oct) 1918.

5 Acuña, M., and Bazán, F. La enfermedad de Recklinghausen en el niño, *Semana méd* **2**:813-833 (Oct 9) 1924.

6 Gardner, W. J., and Frazier, C. H. Bilateral Acoustic Neurofibromas, *Arch Neurol & Psychiat* **23**:266-302 (Feb) 1930.

7 Pende, N. Sistema nervoso simpatico e glandole a secrezione interna, distrofie endocrino-simpatiche, *Tommasi* **4**:732-738, 1909, *Patologia dell'apparecchio surrenale e degli organi parasimpatici*, Milan, Società editrice libraria, 1909, *I nuovi orizzonti della fisiopatologia delle secrezioni interne*, *Med ital* **8**:129-132 and 153-157, 1910.

8 The translations from Pende are from exact quotations found in Muto's article (*Riv di pat nerv* **15**:656-670, 1910). The original sources were not available.

uterine during the period of growth, and (2) an accidental factor, such as shock, trauma, toxins or infection, which through its effects on the endocrine-sympathetic system acts as a stimulus to embryonal elements of the autonomic system in the skin

Much the same ideas were expressed by Lyon,⁹ who concluded that the various clinical symptoms, such as fatty deposit, Dercum's syndrome, the lipomatoses and "adipositas cerebialis," are essentially identical, being only variations of a common morbid process "They all show a tendency to be characterized by constitutional symptoms of wide variety including especially psychic, sensory, motor, vasomotor, secretory, and trophic manifestations"⁸

Minor Etiologic Factors—The incidence of the tumors has no particular sex preponderance The lesions may be present at birth or appear at puberty or during pregnancy The last observation is discussed at greater length in another section of this report The question of irritation is one which has often been a point of discussion There are numerous instances on record in which tumors have developed after local trauma, surgical procedures or prolonged irritation

PATHOGENESIS

Ewing,¹⁰ writing on the origin of fibromas, stated that the exact point of origin is still undetermined That many of them arise from misplaced islands of tissue according to Cohnheim's theory is probable Other fibromas may depend on local irritation and disturbances of nutrition In a third group, the clinical features point to a congenital or local predisposition, of which multiple neurofibromas is the best example It is especially in the second and third etiologic classes that one encounters the less definite tumor-like processes which are sometimes difficult to classify and in which one must recognize the cumulative influences of inflammations and chronic disturbances of nutrition augmenting the passage of inflammatory into self-perpetuating neoplastic processes Von Recklinghausen stated the belief that the mollusum fibrosum arises from the cutaneous nerve filaments He traced degenerating nerve fibers in several characteristic cases and stated that all these tumors arise from nerve trunks or filaments This point, however, has occasioned debate for many years The problem was considered solved when Masson¹¹ did his epochal work on neural growths Masson

9 Lyon, I P Adiposis and Lipomatosis, Considered in Reference to Their Constitutional Relations and Symptomatology, *Tr A Am Physicians* 24 409-501, 1909

10 Ewing, J Neoplastic Diseases, Philadelphia, W B Saunders Company, 1919, p 151

11 Masson, P Recklinghausen's Neurofibromatosis, Sensory Neuromas and Motor Neuromas, in Contributions to the Medical Sciences in Honor of Dr Emanuel Libman, New York, International Press, 1932

and other disciples of the French school stated the belief that the tumors arise from the cells of the sheath of Schwann and are therefore ectodermal in origin. The other leading school of thought, championed by Penfield,¹² Rhoads and Van Wagenen¹³ and others, adheres to the dictum of origin in connective tissue. Their work supports the mesodermal origin of the tumors from the connective tissue sheath of nerves (perineurium). A suggestive point in favor of connective tissue origin was brought forth by Hosoi,¹⁴ who presented a series of cases in which 13 per cent of Recklinghausen's tumors underwent sarcomatous transformation (i. e., a connective tissue malignancy). Regardless of the view adopted, the microscopic appearance is similar to that of other nerve tumors. The tissue has an irregularly woven reticulated appearance with superimposed palisades and whorls of the perineural type. With the use of special stains (Masson's trichrome), nerve fibrils are seen passing through the nodule. The cells are usually long and slender with elongated nuclei. The principal distinction between tumors of the nerve roots and those of the peripheral nerves lies in the fact that the nerve fibers of the root tumors run around the capsule instead of penetrating the center of the growth. The somewhat similar picture encountered in the nevus and the malignant melanoma, especially in the pigmented type, confirms the relation observed clinically between these tumors. The coexistence of melanoma of the iris with neurofibroma, as noted by Goldstein and Wexler¹⁵ and others, still furthers the supposition. The suggestion has been advanced that all pigmented tumors of this group are closely related (nevus, melanoma, neurinoma and neurofibroma). Certainly they are similar pathologically, and clinically they have been noted to coexist. An additional association, namely that of acanthosis nigricans (which has been noted to occur with malignant melanoma and other invasive tumors), should also be kept in mind.

CUTANEOUS CLASSIFICATION

Weber¹⁶ in 1909 suggested this classification: (1) plexiform neuroma, unaccompanied by multiple molluscosus tumors of the skin and with or without cutaneous pigmentation, (2) multiple molluscosus tumors of the skin, without obvious neurofibromatosis of the nerve trunks and

12 Penfield, W. Tumors of the Sheaths of the Nervous System, *Arch Neurol & Psychiat* 27:1298-1308 (June) 1932.

13 Rhoads, C. P., and Van Wagenen, W. P. Observations on the Histology of the Tumors of the Nervus Acusticus, *Am J Path* 4:145-152, 1928.

14 Hosoi, cited by Rhoads and Van Wagenen¹³.

15 Goldstein, I., and Wexler, D. Melanosis Uvae and Melanoma of Iris in Neurofibromatosis (Recklinghausen), *Arch Ophth* 3:288-296 (March) 1930.

16 Weber, F. P. Cutaneous Pigmentation as an Incomplete Form of Recklinghausen's Disease, *Brit J Dermat* 21:49-53, 1909.

with or without cutaneous pigmentation, (3) pigmentation of the skin, not (at least as yet) accompanied by obvious neurofibromatosis of the nerve trunks or molluscous tumors (cutaneous neurofibroma), and (4) anomalous neurofibromatosis complicated by the coexistence of bony or papillomatous changes

A more useful and inclusive grouping is the following

Neurofibromatosis

1 Molluscum fibrosum soft pasty elevation covered by normal skin. There may be hundreds of tumors present

2 Achnoehordon soft pedunculated fibroma which occurs on the head, neck and shoulders of adults and elderly people. On involution, a small hernial sac is left behind

3 Plexiform neuroma elongated and diffuse fibroma confined to the skin along the course of one or more adjacent nerves or nerve plexuses and usually distributed along the trigeminal (fifth) and upper cervical nerves

4 Atypical neurofibroma¹⁷ single or multiple firm hard peripheral tumors sometimes found in association with the nerve roots. They may vary from grayish white to dark red, purple, blue and brown. The tumor produces symptoms merely because of its size, rarely ulcerates and may undergo involution or completely disappear and show surface atrophy. It is freely movable laterally but not in the direction of the nerve. Traction on the growth occasionally produces radiating pains along the course of the involved nerve. It is of clinical importance because it is frequently confused with other tumors of the skin. The differential diagnosis depends on the clinical signs and pathologic changes

5 Fibroma durum,¹⁸ or noduli cutanei¹⁹ growth closely resembling the atypical neurofibroma clinically in that it is a firm, semiglobular tumor which occurs on the buttocks and extremities and is usually insensitive. The differential features are the absence of neural elements in this type of lesion. In addition, it was definitely stated that the fibroma durum is a result of trauma, as from insect bites or as a reaction around foreign bodies. No such etiologic factors play a part in the development of atypical neurofibromas

6 When the enlargement of the nerve trunk is more uniform and the familial element is prominent, Bielschowsky²⁰ applied the name "familial intestinal hyperkeratotic neuritis." This subdivision seems unnecessary

17 Levin, O. L., and Tolmach, J. Atypical Form of Neurofibroma, New York State J. Med. **27** 819 (Aug. 1) 1927

18 Unna, P. G. Fibroma Simplex, in The Histopathology of the Diseases of the Skin, translated by N. Walker, New York, The Macmillan Company, 1896, p. 836

19 Arning, E., and Lewandowski, F. Noduli cutanei, eine bisher wenig beobachtete Hautaffektion, Arch. f. Dermat. u. Syph. **110** 3-14, 1911

20 Bielschowsky, M. Familiäre hypertrophische Neuritis und Neurofibromatose, J. f. Psychol. u. Neurol. **29** 182, 1922

7 Elephantiasis neuromatosa an ill defined wrinkled overgrowth of the skin, usually pendulous and rarely so gigantic as to give rise to a circus monstrosity (Treves's elephant man) This growth is most commonly unilateral and frequently has its origin in the orbitotemporal region Harbitz²¹ wrote a valuable article on the allied condition of elephantiasis in connection with generalized neurofibromatosis He reported the case of a woman, a mongolian imbecile, with an elephantiasis-like growth of the whole thigh and generalized cutaneous tumors The characteristic mongolian appearance had developed at puberty. Perthes²² reported a similar case and detailed the literature of related conditions Thomson's²³ monograph has a particularly fine illustration of the condition Weber mentioned patients with the condition accompanied by bony overgrowth, of whom the "elephant man" described by Sir Frederick Treves²⁴ is the most extreme example

Formes frustes Recklinghausen's disease without tumor formation.

In 1898 Feindel and Oppenheim²⁵ first described what they termed the "incomplete form" of Recklinghausen's disease Weber also directed attention toward the incomplete or abortive type of the disease The cutaneous lesions consist of pigmented spots, but there is no tumor formation Trimble²⁶ in 1911 and Levin²⁷ in 1921 also referred to this type In 1926 Wise and Eller²⁸ reviewed the literature and added 3 cases in which the cutaneous manifestations consisted solely of pigmented spots They advanced the observation that the "formes frustes" usually occur in children of parents with typical neurofibromatosis The name incomplete or abortive Recklinghausen's disease, which has often been applied to this form, is based on the assumption that tumors will eventually appear. We wish to stress the frequent occurrence of this form of the disease and cannot urge too strongly on the physician the implication of glandular derangement connotated by its presence

21 Harbitz, F Multiple Neurofibromatosis, Arch Int Med 3:32-65 (Feb) 1909

22 Perthes, G Ein Fall von Fibroma molluscum, vorwiegend der linken Hand mit Steigerung der Knochenwachsthums, Deutsche Ztschr f Chir 63 103-110, 1902

23 Thomson, H A On Neuroma and Neuro-Fibromatosis, Edinburgh, Turnbull & Spears, 1900

24 Treves, F A Case of Congenital Deformity, Tr Path Soc London 36: 494-498, 1884-1885

25 Feindel, E., and Oppenheim, M Sur les formes incomplètes de la neurofibromatose, Arch gén de med 2 77, 1898

26 Trimble, W B Remarks on Neurofibromatosis (Fibroma Molluscum or von Recklinghausen's Disease), New York M J 93 358-360 (Feb 25) 1911

27 Levin, O L Recklinghausen's Disease Its Relation to the Endocrine System, Arch Dermat & Syph 4:303-321 (Sept) 1921

28 Wise, F, and Eller, J J Recklinghausen's Disease Without Tumor Formation Incomplete or Abortive Forms of Disease, J A M A 86 86-90 (Jan 9) 1926

ASSOCIATED SYMPTOMS

Besides the cutaneous features of Recklinghausen's disease, particularly in those cases characterized by decided pigmentation, there is frequently seen a more or less complete syndrome indicative of dysfunction of the glands of internal secretion. This picture may be so striking as to suggest a diagnosis of insufficiency of the adrenal glands (Addison's disease) as well as other metabolic dystrophies. The findings may include any or all of the following:

Sensory Disturbances—Among the sensory disturbances are arthralgic pains, generally localized in the lumboabdominal region and the calves and hyperesthesia.

Motor Disturbances—These disturbances consist of vertigo, motor incoordination, augmentation of reflexes, diminution of muscular force and asthenia, sometimes progressive to death. Landowski²⁹ stated, "What dominates these patients is a state of general depression or torpor similar to that of Addison's disease. They can hardly move themselves—walking is painful—the slightest movement is a labor. All intellectual effort is fatiguing. The face is dull and stupid, the body bent, thin, and meager."

Psychic Symptoms—Difficulty in learning at school is most commonly mentioned, other symptoms are apathy, indifference, stammering, loss of memory and sometimes imbecility and idiocy of the cretinoid type. The adenoid facies has been noted. Charpentier³⁰ stated that in 63 per cent of the cases Recklinghausen's disease is accompanied by psychic defects symptomatic of mental degeneracy. As is obvious, these symptoms are quite distinct from those present in the same disease when the fibromatous growths have invaded the cerebrospinal nerves or even the central nervous system itself. Gordon³¹ in 1938 presented a case in which there were Recklinghausen's tumors on the body and the eyebrow. In addition there was involvement of two cranial nerves and of the spinal cord. He stated that cortical involvement might lead to idiocy, defective memory, psychoses, convulsions, hemiplegia and tuberous sclerosis. The association of tuberous sclerosis, adenoma sebaceum and Recklinghausen's disease will be discussed in another part of this paper.

Defects in Development and Faulty Osseous Growth—Stigmas of degeneracy, usually congenital, such as nevi, arched palate, facial asym-

29 Landowski, L. La neuro-fibromatose généralisée, *Gaz d hôp* 69 946 1896

30 Charpentier, J. Maladie de Recklinghausen et psychose periodique, *Encephale* 5 460-465, 1910

31 Gordon, A. Diffuse Polymorphous Neurofibromatosis, with Unusual Localization and Involvement of Central Nervous System, *Arch Dermat & Syph* 37 983-986 (June) 1938

metry, prognathism, malformation of ears, syndactylism, badly spaced teeth and changes in the nails, may be present. The adult, usually of small stature, shows lack of complete development, infantilism, faulty growth of the hair, dwarfism and sexual underdevelopment. Stahnke³² in 1922 noted the bony changes associated with neurofibromatosis and stated that they were not a casual coincidence but formed a part of the clinical picture. In addition he stated that the changes were in the nature of congenital defects, thereby demonstrating that Recklinghausen's disease must be accepted as a malformation in the wider sense. The osseous changes were further classified by Brooks and Lehman³³ in 1924. They maintained that the bony abnormalities were a common and characteristic accompaniment of the cutaneous changes and their work has since been corroborated by numerous investigators. Their statistics placed scoliosis at the head of the list of bony changes. The type of scoliosis may be either a mild curve due to unequal length of the legs or severe kyphoscoliosis due to local bony changes. They also noted subperiosteal cysts (not to be confused with osteitis fibrosa cystica), and Lehman³⁴ later emphasized the presence of cystic areas in the skull. The bony cysts may actually be neurofibromas developing in the periosteum of the long bones, each covered by a thin bony shell. Almost any bony abnormality due to invasion or erosion of the bone by the growth may be encountered. They are due not only to endocrine effects but to local disturbances of innervation or of tumor growth.

Defects in Hearing—The association of deafness with Recklinghausen's disease has been noted by many observers, notably Verocay³⁵ and Cushing³⁶. The usual cause is a bilateral acoustic neurofibroma. While acoustic neuromas are common brain tumors, they are usually single. When bilateral tumors exist they are more often indicative of the widespread cutaneous neurofibromatosis. The symptoms of deafness and increased intracranial pressure are usually not manifested until adult life, although Berggrun³⁷ reported the development of

32 Stahnke, E. Ueber Knochenveränderung bei Neurofibromatose, Deutsche Ztschr f Chir 168:6-18 (Jan) 1922

33 Brooks, B., and Lehman, E. P. Bone Changes in von Recklinghausen's Neurofibromatosis, Surg, Gynec & Obst 38 587-595 (May) 1924

34 Lehman, E. P. Recklinghausen's Neurofibromatosis and the Skeleton, Arch Dermat & Syph 14 178 (Aug) 1926

35 Verocay, J. Zur Kenntnis der Neurofibrome, Beitr z path Anat u z allg Path 48 1-69, 1910

36 Cushing, H. Tumors of the Nervus Acusticus, Philadelphia, W. B. Saunders Company, 1917

37 Berggrun, E. Ein Fall von allgemeiner Neurofibromatose bei einem 11jährigen Knaben Arch f Kinderh 21:89, 1896

symptoms in a child of 11 years Cushing also reported a series of 18 cases of glioma of the optic chiasm, in some of which the disease produced blindness and in 5 of which it was associated with neurofibromatosis

Few patients have all the symptoms mentioned in the foregoing paragraphs However, many do possess a sufficient number of them to present an unmistakable syndrome which various French writers, notably Charpentier, have called the classic picture of Recklinghausen's disease, regarding the psychic symptoms as practically habitual

ENDOCRINE-AUTONOMIC RELATIONS THE ENDOCRINE GLANDS

A somewhat detailed account of characteristic cases is here presented, since, except in the article of Elliott and Beinfeld³⁸ (1914) which attempts to connect Recklinghausen's disease with status thymolymphaticus, there has been no review in English of the work of many foreign writers, notably French and Italian, who have endeavored to establish a connection between Recklinghausen's disease and glandular imbalance Such a connection, although widely accepted on the Continent, has been generally overlooked in the American literature Although many cases are reported in which the authors' interests were so entirely dermatologic as to exclude most other information, and although there are others in which the authors state that no nervous or functional symptoms were present, there is also considerable literature reviewing cases in which involvement of the pituitary, thyroid, adrenal and sexual glands is unmistakable The picture is one of general glandular dystrophy, with varying emphasis on different glands

Sex Glands—It is significant that in many cases the condition is influenced by the onset of menstruation, by pregnancy and by the menopause Pigmentation and tumors usually appear first or rapidly increase between the twelfth and the eighteenth years, it is a common statement in the histories of both males and females that the disease developed at the onset of puberty

Menstrual anomalies figure in certain cases, as in Meige and Feindel's³⁹ case of myxedematous infantilism, in which menstruation was barely established, and in a similar case reported by Orzechowski,⁴⁰ that of a girl of 18 with primary amenorrhea

38 Elliott, C A, and Beinfeld, A F Generalized Neurofibromatosis (von Recklinghausen's Disease) Report of a Case Showing a Superficial Resemblance to Hodgkin's Disease, *J A M A* **63** 1358-1362 (Oct 17) 1914

39 Meige, H, and Feindel, E Infantilisme myxodematoux et maladie de Recklinghausen, *Rev neurol* **11** 857, 1903

40 Orzechowski, K, and Nowicki, W Zur Pathogenese und pathologischen Anatomie der multiplen Neurofibromatose und der Sclerosis tuberosa (Neurofibromatosis universalis), *Ztschr f d ges Neurol u Psychiat* **11** 237-397, 1912

Bourcy and Laignel-Lavastine⁴¹ reported a case in which tumors first developed at the age of 15, more appeared after marriage and immediately after the menopause a molluscum pendulum appeared. Hirst⁴² and Sutton⁴³ had cases in which tumors appeared during but not between pregnancies. In Sutton's case the tumors shrank up after the first delivery, but some of those of the second pregnancy persisted.

Bérard⁴⁴ reported a case in which an enormous cyst of the ovaries was associated with multiple cutaneous and subcutaneous tumors. After ovariectomy, the tumors progressively disappeared until at the end of three years only the smallest remained. Pascalis⁴⁵ and Oddo⁴⁶ reported similar cases. Sharpe and Young⁴⁷ reported several cases in which tumors developed or were aggravated by pregnancy. They prognosticate an interesting pathogenesis. In a typical case, the child at the age of 3 years is taken to a pediatrician because of pigmentation of the skin. At the age of 7 years, she is taken to an orthopedist for scoliosis. At the age of 15 she visits a dermatologist for treatment of cutaneous tumors. When she is between 20 and 30, her obstetrician is asked why the tumors and pigmentation increase with pregnancy. At 35, she consults an otologist for beginning bilateral deafness. And when she is 50, a surgeon observes malignant transformation of the breast. Of course, the prognosis is not as gloomy as in this illustration, but the sequence noted is of theoretic interest. Sharpe and Young stated that pregnancy was the most potent factor leading to progression of the lesions in their series. They stated the belief that pregnancy should be avoided if the disease is to be controlled.

Many of the conditions in males also develop or become active at puberty, and an incomplete or delayed sexual development, cryptorchidism and lack of pubic hair and other characteristics were mentioned in cases in which there were no other obvious signs of glandular involve-

41 Bourcy, P., and Laignel-Lavastine. Autopsie d'un cas de maladie de Recklinghausen, *Bull et mém Soc méd d hôp de Paris* 22:21-26, 1905.

42 Hirst, B. C. Etiological Influence of Pregnancy on Molluscum, *Am J M Sc* 147:419, 1914.

43 Sutton, R. L. A Clinical Note on Fibroma Molluscum Gravidarum Fibrosum, *Am J Obst* 63:256, 1911.

44 Bérard, L. Ancien cyste de l'ovaire et tumeurs cutanées multiples, *Bull Soc chir de Lyon* 5:15 (Nov 13) 1902.

45 Pascalis, G. Molluscum pendulum volumineux de la cuisse au cours d'une maladie de Recklinghausen, *Bull et mém Soc anat. de Paris* 13:102, 1911.

46 Oddo, C. Maladie de Recklinghausen avec pigmentation des muqueuses, *Rev neurol* 13:412-415, 1905.

47 Sharpe, J. C., and Young, R. H. Recklinghausen's Neurofibromatosis. Clinical Manifestations in Thirty-One Cases, *Arch Int Med* 59:299-328 (Feb) 1937.

ment Harbitz ⁴⁸ reported the case of a man of 28 with cryptorchidism who had shown pigmented areas since birth and in whom generalized cutaneous fibromas had developed at the age of 15 Bénaky ⁴⁹ had a patient, a man aged 40, with congenital pigmentation, generalized neurofibromatosis and molluscum pendulum, as well as skeletal deformities and sexual underdevelopment Guinon and Reubsæet ⁵⁰ described the case of a boy, aged 12 years, with pigmentation from birth, progressively growing tumors, stupidity, adenoid facies and lack of testicular development There were other reports ⁵¹ of similar conditions in young boys

Pituitary Gland—It is to be expected that Recklinghausen's disease should be associated with hypophysial dysfunction, as there seems to be some connection between hypopituitarism and certain tumorous formations that are apparent in conditions like multiple lipomatosis

Evidences of pituitary abnormality in Recklinghausen's disease are found in many patients with a partial acromegalic tendency, such as prognathism or cheiromegaly, and in the confluent elephantiasic form of the disease, as well as in the few cases in which generalized fibromas appear with acromegaly ⁵² The cases of de Castro and of Wolfsohn and Marcuse ^{52b} both showed typical acromegaly The condition in both was characterized by nervous phenomena, headache, pains in the limbs, psychic depression and general asthenia Wolfsohn and Marcuse found that roentgenoscopic examination of the sella turcica showed an increase of measurements from normal to abnormal within three months'

48 Harbitz, F Multiple Neurofibromatosis, Arch Int Med 3 32-65 (Feb) 1909

49 Bénaky Neuro-fibromatose généralisée avec molluscum pendulum de la moitié droite de la face et ptosis de l'oreille, Ann de dermat et syph 5 977-982, 1904

50 Guinon, L, and Reubsæet, A Un cas de maladie de Recklinghausen fruste, Bull Soc pediat de Paris 9 263-267 (June 16) 1907

51 Preiser, S A, and Davenport, C B Multiple Neurofibromatosis (von Recklinghausen's Disease) and Its Inheritance, with Description of a Case, Am J M Sc 156 507-540, 1918 Elliott and Beifeld ³⁸ Poisson and Lebat Maladie de Recklinghausen, Gaz méd-chir, Nantes, May 3, 1918, p 357 Little, E G G Case of von Recklinghausen's Disease, Proc Roy Soc Med (Sect Dermat) 2 38, 1909, Brit J Dermat 21 253, 1909

52 (a) Feindel, E, and Froussard, P Dégenescence et stigmates mentaux, malformation de l'ectoderme, myoclonie épisodique, acromégalie possible, Rev neurol 7 46-54, 1899 Piolet, P Neuro-fibromatose généralisée, Gaz d hôp 75 1345-1350, 1902 Cushing, H The Pituitary Body and Its Disorders, Philadelphia, J B Lippincott Company, 1912, p 148 Nicolas, J, and Favre, M Acromégalie et maladie de Recklinghausen, Lyon med 114 786, 1910 (b) de Castro, A Sur la coexistence de la maladie de Recklinghausen avec l'acromégalie Nouv iconog de la Salpêtrière 25 41-44, 1912 Wolfsohn, G, and Marcuse, E Neurofibromatosis und Akromégalie, Berl klin Wchnschr 49 1088, 1912

time Jeanselme⁵³ recorded an instance of accompanying narrowness of the sella turcica Breton,⁵⁴ in a case of Addison's syndrome, observed at necropsy an enlarged pituitary gland and a sella turcica filled with lymphoid tissue Spillman⁵⁵ observed a tumor of the sella turcica, and Mosse and Cavalié,⁵⁶ an enlarged and hard hypophysis Tucker⁵⁷ (1924) noted acromegalic manifestations in 3 of 9 cases, in 2 of them there was a large sella turcica Sisto⁵⁸ (1929) observed 1 case of acromegaly with neurofibromatosis Vizioli⁵⁹ (1930) reported a case of acromegaly and neurofibroma with an enormous tumor of the occipital region De Castro⁶⁰ (1934) and Schlesinger noted the association of acromegaly with Recklinghausen's disease Although the array of cases is rather convincing, it should be noted that Atkinson⁶¹ (1932) in a study of 768 cases of acromegaly observed only 4 cases of Recklinghausen's disease

Generalized neurofibromas associated with Frohlich's syndrome, dystrophia adiposogenitalis, was reported by Lier⁶² in a boy aged 9 years Roentgenoscopic examination showed evidence of a tumor close to the hypophysis Laignel-Lavastine and Ravier⁶³ (1927) noted a familial case of Recklinghausen's disease with associated dwarfism

Thyroid—Instances of cretinism in patients with Recklinghausen's disease were recorded by Adrian,⁶⁴ Strohmeyer⁶⁵ and Schuh⁶⁶ Schiff-

53 Jeanselme, E Anomalies de l'appareil visuel, de l'intelligence et du squelette associées à la neurofibromatose généralisée, Bull et mém Soc méd d hôp de Paris 31:1136-1139, 1915

54 Breton, A La neurofibromatose généralisée, Rev gén de clin et de therap 17:17-20, 1903

55 Spillman Neurofibromatose et tumeurs cérébrales, Gaz hebdomadaire de médecine 5 320, 1900

56 Mosse, A, and Cavalié Tumeurs multiples de l'encéphale et de la moelle allongée, Neurofibromatose centrale, Gaz hebdomadaire de médecine 2:789, 1897

57 Tucker, B R Von Recklinghausen's Disease, with Especial Consideration of the Endocrine Connection, Arch Neurol & Psychiat 11 308-320 (March) 1924

58 Sisto, F Acromegalia e neurofibromatosi di Recklinghausen, Minerva medica (pt 1) 9 97 (Jan 20), 128 (Jan 27) 1929

59 Vizioli, E Morbo di Recklinghausen, acromegalia frusta ed enorme tumore della regione occipitale, Riv di pat nerv 35 96-100 (Feb) 1930

60 de Castro, A Acromegalia et maladie de Recklinghausen, Rev neurol 1:39 (Jan) 1934

61 Atkinson, F R B Acromegaly, London, John Bale Sons & Danielsson, Ltd, 1932

62 Lier, W Ueber Neurofibromatose, Ztschr f klin Med 80 261-269, 1914

63 Laignel-Lavastine, P, and Ravier, J Un cas de maladie de Recklinghausen familiale avec nanisme, Bull et mém Soc méd d hôp de Paris 51:1112-1115 (July 14) 1927

64 Adrian Centralbl f d Grenzgeb d Med u Chir 6:461, 1903

65 Strohmeyer, cited by Adrian⁶⁴

66 Schuh, F Ueber die Erkenntnis der Pseudoplasmen, Vienna, L W Seidel, 1851, Pathologie und Therapie der Pseudoplasmen, Vienna, W Braumüller, 1854, cited by Adrian⁶⁴

nei observed true cretinism in 2 brothers with the disease (Julien) Ottolia⁶⁷ regarded his patient as cretinoid Debove⁶⁸ reviewed the case history of a man with multiple cutaneous tumors, growths along the course of the nerves and generalized pigmentation, in conjunction with thyroid infantilism

Myxedematous conditions were found in the cases of Meige and Feindel and of Pic and Rebattu⁶⁹ At necropsy Bourcy and Laignel-Lavastine observed, among other glandular lesions, a typical fibrous goiter with bloody infiltration and diminution of colloid Muto⁷⁰ also found changes in the thyroid at necropsy Ehrmann⁷¹ observed a small thyroid in 1 case and no gland in another Hallopeau and Ribot⁷² reported typical pigmentation and tumors in a woman in whom exophthalmic goiter was making its appearance Gordon⁷³ (1929) reported a case of myxedema with neurofibromatosis

Parathyroids—Schlesinger⁷⁴ in 1911 recorded the first case of neurofibroma associated with tetany Mariante and Maciel⁷⁵ (1932) noted a relation between both of Recklinghausen's diseases (neurofibromatosis and osteitis fibrosa cystica) and advanced the theory that disturbance in the calcium balance plays a role in the origin of both diseases The bony changes in both may be due to an excess of calcium in both blood and urine, thereby leading to progressive excretion of calcium and decalcification of bone Norsa⁷⁶ (1934) reported a case of hyperparathyroidism, osteitis fibrosa cystica and neurofibromatosis Chinag-

67 Ottolia, D Considerazioni sopra un caso di morbo di Recklinghausen, *Riforma med* 24 1243-1247, 1908

68 Debove Sur un cas de neuro-fibromatose de Recklinghausen, *J de med et chir prat* 76 566-568, 1905

69 Pic and Rebattu Un cas de maladie de Recklinghausen, *Lyon med* 108 636-643, 1907

70 Muto, A Contributo allo studio del morbo di Recklinghausen, *Riv di pat nerv* 15 656-670, 1910

71 Ehrmann, S Zwei Falle von Neurofibromatose, *Wien klin Wchnschr* 17 139-140, 1904

72 Hallopeau, H, and Ribot, A Un cas de maladie de Recklinghausen avec predominance des troubles pigmentaires et volumineuse tumeur profonde, *Ann de dermat et syph* 3 613-615, 1902

73 Gordon, M B Endocrine Consideration of Recklinghausen's Disease Report of Case with Associated Childhood Myxedema, *Endocrinology* 13 553-563 (Nov) 1929

74 Schlesinger, H Multiple Neurofibroma der peripheren Nerven und der Nervenwurzeln, mit Beinphanomen, *Mitt d Gesellsch f inn Med u Kinderh* 10 124-125, 1911

75 Mariante, T, and Maciel, P Doenças di Recklinghausen e metabolismo calcico, *Rev radiol clin* 1-332-341 (June) 1932

76 Norsa, G Iperparatiroidismo, osteite fibro-cistica generale e neurofibromatosi, *Gazz d osp* 55 1221-1223 (Oct 7) 1934

lia⁷⁷ (1936), as well as Cohen and Douady⁷⁸ (1936), observed patients with hyperparathyroidism and neurofibromatosis. They also stated the belief that hypercalcemia had a possible etiologic significance and nosologic relation. Cohen and Douady presented 1 case and reviewed several others with both Recklinghausen's diseases. They stated that hyperparathyroidism is but one of the endocrine abnormalities so frequently encountered in neurofibromatosis and that the bony changes seen so often are due to involvement of the parathyroid. They have observed kyphoscoliosis, osteoporosis and spontaneous fractures in both diseases. The only objection to this theory, according to the authors, is that a tumor of the parathyroids has never been demonstrated in the postmortem examination of persons with neurofibromas. However, only few autopsies have been performed, and the need for specialized technic and the ability to demonstrate this type of tumor is obvious. How often have cases of undoubted osteitis fibrosa cystica come to the autopsy table, with the tumors of the parathyroid abnormally placed or too small to be demonstrated? We believe that the involvement of the parathyroids is another proof of glandular involvement and that it may well be a factor in the production of bony changes, a factor that is frequently overlooked.

Adrenals—A far from complete review of the literature has disclosed about 50 cases in which a so-called Addisonian syndrome, entirely or partially developed, indicated adrenal involvement. Many other cases characterized by these symptoms would doubtless have been found if the reporter's interest had not been entirely taken up by cutaneous and nerve tumors. We believe that in a great majority of cases of Recklinghausen's disease there will be found certain indications of glandular insufficiencies. A few typical cases showing the clinical picture of Addison's syndrome are detailed.

1 (Pic and Rebattu, 1907) A man aged 47 complained of progressive asthenia, multiple cutaneous molluscous tumors, neurofibromas along the course of the spinal nerves, widely scattered café-au-lait patches from birth, deep brown punctiform pigmentation of the lower part of the legs, extreme kyphoscoliosis and a myxedematous appearance, caused by infiltration of the integument down to the shoulders, his intellectual faculties, formerly intact, were weakened. The extreme asthenia was accompanied by hypotension and vasomotor changes.

2 (Ottolia, 1908) A small underdeveloped cretinoid man had such symptoms as scoliosis and deformation of bones of the head, generalized tumors, pigmentation all

77 Chinaglia, A. Contributo allo studio della neurofibromatosi cutanea nei rapporti con lesioni ossee—Calcemia—Turbo endocrine, Arch ital di chir **43** 315-333, 1936.

78 Cohen, R, and Douady, D. Coexistence des deux maladies de Recklinghausen chez un sujet, leurs liens nosologiques, Presse méd **44** 2063-2064 (Dec 19) 1936.

over the body (including the buccal mucous membranes), intellectual inferiority, slowness of movements and diminished sensibilities

3 (Thiebièrge,⁷⁹ 1898) A woman aged 56 had had small and large pigmented patches, identical with those of neurofibromatosis, over her trunk since birth. There were no tumors, but she had extreme asthenia for two years. With the onset of this condition there occurred generalized discoloration of the skin of the face and body, alteration of character, melancholia and loss of memory.

4 (Thiebièrge) A man aged 50 had typical tumors, deep brown pigmentation and gastric symptoms, progressive to death.

5 (Jullien,⁸⁰ 1910) A woman aged 43 had had tumors at the age of 2½ years, pigmentation and bronzing of the face at 7 years, irregular menstruation, and headaches, gastric distress and vomiting at puberty. At the time of writing she presented pigmentation of the neck and hands, an Addisonian mask, a large pigmented patch on the mucous membrane on the inside of the cheek and lumboabdominal pains, she was quickly fatigued. There was a recurrence in situ of a pleomorphic neuroma removed from the hypogastrium.

6 (Kahn,⁸¹ 1910) A man aged 42 was presented. At the age of 33 he had had pigmentation and multiple tumors. Since that time there had been anorexia, vomiting, lumbar pains, exophthalmos, asthenia and pulmonary tuberculosis. Kahn reported this case as one of Addison's disease, but the tumors, the absence of pigmentation on the mucous membranes and the observations at necropsy failed to support the diagnosis.

Such is the clinical picture, one of degeneracy and lack of resistance. The exciting causes which bring into activity the underlying tendencies (congenital, hereditary or familial) in these persons may be any one of many, such as puberty, pregnancy, menopause, trauma or infection, the stimulus may vary, but the inherent tendency is constant. In a previous paper, a report of cases in which necropsies were performed was given. Twelve of these were cases in which a more or less complete Addisonian syndrome had been found, 2 cases lacked such phenomena. In 12 of the cases, or 85 per cent, including the 2 without Addison's syndrome, involvement of the adrenals and other glands was found. In 2 cases, in both of which there were clinical indications of adrenal involvement, there were only minor histologic changes in the glands.

The proof of glandular dystrophies offered by changes in the glands found at necropsy, even though changes were found in so large a proportion of the few cases studied, is interesting rather than convincing, even in undoubted Addison's disease the adrenals are occasionally intact at necropsy. Furthermore, as is well known, a general dysfunc-

79 Thiebièrge, G. Un cas de maladie de Recklinghausen sans fibromes cutanés ni fibromes nerveux, *Bull et mém Soc méd d hôp de Paris* 15 143-149, 1898.

80 Jullien, A. Contribution à l'étude de la neurofibromatose généralisée (Maladie de Recklinghausen), Thesis, Paris, no 266, 1910.

81 Kahn, I. N. Report of a Case of Molluscum Fibrosum, Addison's Disease and Pulmonary Tuberculosis, *New York M J* 2 114, 1910.

tion of the glandular system may be clinically manifest for a considerable time before any great changes appear in the structure of the glands. No stronger proof of glandular involvement is needed than the clinical conditions shown. However, as the necropsy examinations are of interest, they are herein detailed, together with a case in which a tumor of the adrenals was found in a living subject afflicted with neurofibromatosis.

1 (Chauffard,⁸² 1896) A man aged 37 presented pigmentation, neurofibromatosis and increasing digestive disturbances. Death was due to cachectic marasmus. A necropsy revealed a voluminous adenomatous tumor of cortical origin, which involved the pancreas, adrenals and lymphatic ganglions and in which there was capsular degeneration. The absence of the tuberculous transformation of the adrenals, characteristic of Addison's disease, was noted.

2 (Branca,⁸³ 1897) A man aged 43, an alcoholic addict, had multiple pigmented nevi and molluscous tumors, he was cachectic and tuberculous, and his intelligence and memory had diminished. The condition was diagnosed as Marie's disease. At necropsy the kidneys were red, hard and small, there were cysts and an adhesive capsule. The adrenal capsule was congested. There was no involvement of the sympathetic nervous system.

3 (Marie and Couvelaire,⁸⁴ 1900) The disease developed late in a man, after his hands and feet were frozen. Then followed such symptoms as progressive asthenia, neurofibrosis (which became generalized, with pigmentation), alterations of sensibility, apathy and anorexia. There were extreme skeletal changes, the photographs show appalling progressive kyphosis. Death was due to extreme asthenia. Necropsy revealed osteomalacia and intestinal fibromatosis, the pancreas was sclerotic, the splenic artery extremely sclerosed, the spleen hard, and the adrenal cortex intact.

4 (Merk,⁸⁵ 1905) A man aged 34 (?) suffered from neurofibromatosis with pigmentation, diminished intellect and asthenia. Necropsy showed changes in the left adrenal.

5 (Raymond and Alquier,⁸⁶ 1908) A woman aged 74 had a cutaneous fibroma, with pigmentation, headaches, vertigo and profound asthenia, there were no neuromas. At necropsy the adrenals were occupied by generalized sclerosis, at one point that had escaped sclerosis, there was a hyperplastic nodule of spongocytes. The kidneys were sclerotic. The hypophysis showed alternating layers of sclerosis and hyperplasia.

82 Chauffard, A. Derm-fibromatose pigmentaire (ou neurofibromatose généralisée). Mort par adénome des capsules surrénales et du pancréas, *Bull et mem Soc de med et chir prat de Paris* 76:566-568, 1905.

83 Branca, A. Neuro-fibromatose intestinale, *Bull et mem Soc anat de Paris* 72:166-173, 1897.

84 Marie, P., and Couvelaire, A. Neuro-fibromatose généralisée. Autopsie, *Nouv iconog de la Salpêtrière* 13:26-40, 1900.

85 Merk, L. Ueber die multiple Neurofibromatose, *Arch f Dermat u Syph* 73:139-145, 1905.

86 Raymond, F., and Alquier, L. La maladie de Recklinghausen. Ses variétés nosologiques, *Encéphale* 3:6-35, 1908.

6 (Vignolo-Lutati,⁸⁷ 1911) A man aged 25 had pigmentation at birth, cutaneous tumors at puberty and loss of strength, nausea, vomiting and bronzing of face three years before death. Death was from cachexia. Necropsy showed sclerosis of the adrenals.

7 (Saalman,⁸⁸ 1913) A woman aged 35 had typical Recklinghausen's disease. Death was from pulmonary embolism after operative removal of an elephantiasic tumor from the arm. At necropsy a hypernephroma, originating in an adrenal test, was observed in the liver. The adrenals appeared normal.

8 (Bosquet,⁸⁹ 1913) A man aged 46 had cutaneous and nerve tumors, sexual frigidity, anorexia, pains in the extremities and profound asthenia, his skin was a uniform dirty yellow, as in Addison's disease. Necropsy revealed that the right adrenal was almost entirely transformed into an epithelial tumor, with polymorphic cells and cystic and hemorrhagic formations.

9 (Kawashima,⁹⁰ 1911) A woman in puerperium had multiple cutaneous and nerve tumors and severe kyphoscoliosis. There was a tumor of the adrenal medulla, consisting of atypical hyperplasia of giant multinuclear cells.

THE AUTONOMIC NERVOUS SYSTEM

The views of Pende have been cited. Clarke and Wakefield⁹¹ (1926) stated that the primary pathologic changes of Recklinghausen's disease lie in the sympathetic or parasympathetic nervous system, with the internal secretions playing a secondary role. They presented 2 cases, in 1 of which there was tachycardia and in the other, auricular fibrillation. They stated the belief that the occurrence of tachycardia or bradycardia during the course of the disease is due to actual tumorous involvement of the sympathetic and parasympathetic nerves. This involvement had been noted in several previous postmortem examinations. The authors stated that stimulation, irritation or paralysis of the autonomic nervous system by the growths may produce secondary signs and symptoms of endocrine disease. Rosenthal and Willis⁹² (1936) noted the association of chromaffin tumors with neurofibromatosis.

87 Vignolo-Lutati, C. Recklinghausenschen Krankheit, *Monatsh f prakt Dermat* **52** 51-70, 1911.

88 Saalman. Ueber einem Fall von Morbus Recklinghausen, mit Hypernephrome, *Virchows Arch f path Anat* **211** 424, 1913.

89 Bosquet, T. Maladie de Recklinghausen et capsules surrénales, *Echo med du Nord* **17** 329-332, 1913.

90 Kawashima, K. Ueber einem Fall von multiplen Hautfibromen mit Nebennierengeschwulst. Ein Beitrag zur Kenntnis des sogenannten Morbus Recklinghausen, *Virchows Arch f path Anat* **203** 66-74, 1911.

91 Clarke, G. F., and Wakefield, E. G. Cardiovascular Disease as a Complication of Generalized Neurofibromatosis, *Arch Dermat & Syph* **13** 806-814 (June) 1926.

92 Rosenthal, D. B., and Willis, R. A. Association of Chromaffin Tumors with Neurofibromatosis, *J Path & Bact* **42** 599-603 (May) 1936.

PREGNANCY

Whether pregnancy should be considered by itself or under endocrine changes is debatable. Certain definite glandular changes have been shown⁹³ to occur during pregnancy. The thyroid is enlarged due to parenchymatous changes and increased vascularity. Histologically, glandular hyperplasia is noted. The basal metabolic rate increases, and symptoms of hyperthyroidism grow worse during pregnancy. From this, can it be assumed that the effect of the thyroid secretions on cellular oxidation and metabolism causes the increased growth of fibroma during pregnancy?

The pituitary gland also enlarges considerably with pregnancy. The main enlargement is that of the anterior lobe, which may become almost twice its normal size. Is it then the growth-stimulating principle of the anterior lobe of the hypophysis which is responsible for the enlargement of the tumors?

The ovaries secrete an increased amount of theelin and progesterin during gestation. Theelin is responsible for the growth of the endometrium and together with progesterin affects the growth of the breast. Are these the growth factors which act on neurofibroma?

Few reports are available on changes in the adrenal glands during pregnancy. Fitz-Patrick reported a series of 12 patients with Addison's disease, 5 of whom died during pregnancy. In other words, there was an acute exacerbation of adrenal insufficiency. It has often been stated that after the administration of an extract of the adrenal cortex to patients with Addison's disease the cutaneous pigmentation becomes lighter. Should it be assumed that there is a decreased secretion of cortin during pregnancy which causes the increased pigmentation of the skin? An additional factor has been brought forward by Loeb,⁹⁴ who stated that the decrease in pigmentation in Addison's disease is due to dehydration of the tissue spaces, with stretching of the skin. The inclusion of a disturbance of salt and water metabolism is then another possibility. The question now arises as to the respective importance of the roles played by the different glands. Sharpe and Young stated that pregnancy influences an arrest of embryonic tissue by stimulation of the normal physiologic growth factor, thereby causing increased growth of the tumor. We believe that the factor is indirect and through the various glandular secretions. It is impossible to state which particular hormone is responsible for the major change. In addition, the growing fetus adds its glandular secretions and physiologic effects to those of the mother.

⁹³ Beck, A. C. *Obstetrical Practice*, Baltimore, Williams & Wilkins Company, 1935.

⁹⁴ Loeb, R. F. *The Adrenal Cortex*, J. A. M. A. **104** 2177-2182 (June 15) 1935.

OTHER DISEASES

There have been several reports on the association of Recklinghausen's disease with tuberous sclerosis⁹⁵ The condition is marked by the occurrence of mental deterioration in the first or second year of life, with gradually progressive idiocy⁹⁶ Epileptiform convulsions⁹⁷ may appear later on In about 50 per cent of these cases the condition is associated with adenoma sebaceum In addition, tumors of the kidney (hypernephroma) and of the heart (rhabdomyoma) have been observed Pathologically, various malformations and glial tumors of the brain have been described Microscopically there are spongioblastic-like nests of cells in the central nervous system, which are similar to neurofibromas of the brain and spinal cord Skeer⁹⁸ (1938) described a case of adenoma sebaceum, Recklinghausen's disease and subungual fibromatosis, associated with epilepsy or tuberous sclerosis Patients showing all these stigmas of the disease have been termed "epiloiacs" by the neurologists Skeer stated that in these four diseases there is a tendency toward proliferation of connective tissue He also commented on the frequent clinical association of Recklinghausen's disease with tuberous sclerosis and noted Bielchowsky's observation on the common spongioblastic nature of the two conditions

Although no further contributory influences are described, the association of neurofibromatosis with other diseases is mentioned for the sake of completeness Fleming and Cookson⁹⁹ noted its association with epilepsy and osteoporosis (1 case), and Brocher and Frommel,¹⁰⁰ with periarteritis nodosa (1 case), and Thalmann¹⁰¹ commented on its relation to generalized osteitis deformans

95 Wechsler, I A Textbook of Clinical Neurology, Philadelphia, W B Saunders Company, 1930

96 Brennemann, J Practice of Pediatrics, Hagerstown, Md, W F Prior Company, Inc, 1927, vol 4, pp 18-28

97 Grinker, R Neurology, Springfield, Ill, Charles C Thomas, Publisher, 1934, p 231

98 Skeer, J Adenoma Sebaceum (Pringle), von Recklinghausen's Disease Subungual Fibromatosis Associated with Epilepsy or Tuberous Sclerosis Symptom Complex, Urol & Cutan Rev **42** 110-114 (Feb) 1938

99 Fleming, G W, and Cookson, H A Multiple Neurofibromata Associated with True Angioneurofibroma of the Acoustic Nerve, Jacksonian Epilepsy and Osteoporosis, J Neurol & Psychiat **6** 104-113 (Aug) 1925

100 Brocher, J E, and Frommel, E Periarterite nouvelle en voie de guérison associée à une neurofibromatose familiale Documents cliniques et histologiques, Ann de méd **23** 265-276 (March) 1928

101 Thalmann, W Ueber die Beziehungen zwischen generalisierter Ostitis deformans Paget und Neurofibromatosis Recklinghausen, Virchows Arch f path Anat **283** 148-158, 1932

THERAPY

The logical approach to the treatment of von Recklinghausen's disease is apparently through the medium of opotherapy. The small tumors may be removed by means of electrodessication, while the large tumors may be treated by the same procedure or by surgical intervention. Surgical removal of the tumors is occasionally not advised, as the tissues heal poorly. In addition, tumors may be situated in close proximity to important structures, such as the vagus nerve, and surgical removal might lead to severe shock or even death. Furthermore, the possibility of malignant transformation is an ever present indication for conservatism. We do not feel that the usual manifestations of Recklinghausen's disease are of such severity as to predicate an absolute contraindication toward pregnancy, as has been proposed. Ketcham¹⁰² (1937) suggested trying combinations of thyroid, solution of adrenal cortex and a preparation of the anterior lobe of the pituitary gland to see if they caused any evident changes in growth. If successful results are obtained, the usage of antagonistic preparations, if available, may be useful. If the results are not successful or if the tumors actually shrink in size, thereby showing a deficiency rather than an oversecretion to be the underlying provocative factor, then there are definite therapeutic agents available. The need for controlled experimentation is obvious. Recently, the administration of thiamin chloride (vitamin B₁) in doses of 3 mg or more daily has been suggested. The antineuritic powers of the vitamin may be the reason for its supposed efficacy. The often quoted statement of Harbitz,¹⁰³ "The patients die with the disease and not from it," is a dictum that is so often applied to many cutaneous conditions. The physician should remember that cutaneous growths and abnormalities have a far greater effect through the "psyche" than the "soma." The patient, especially a young woman, can be extremely unhappy from the cosmetic defects of neurofibromatosis.

REPORT OF CASES

The following cases, briefly presented and discussed, were selected to illustrate various phases of von Recklinghausen's disease.

CASE 1—F G, a housewife aged 49, noticed the development of multiple cutaneous nodules after the birth of her last child (at the age of 30). At the age of 48, a swelling appeared on the dorsum of the terminal phalanx of the right ring finger. On admission to the hospital glomus tumor was diagnosed. It was also noted that she had innumerable pinhead-sized to hazelnut-sized, soft and hard brownish and whitish, occasionally pedunculated nodules all over her body. Many small

¹⁰² Ketcham, W M, in discussion on Sharpe and Young⁴⁷

¹⁰³ Harbitz, F. Multiple Neurofibromatosis, Arch Int Med 3 32-65 (Feb) 1909

brownish spots and some large chloasmatic areas were present. The swollen part of her finger was excised, and the pathologic report was glomus tumor.

The condition represents the type known as molluscum fibrosum. The first appearance of the growths during pregnancy is somewhat typical, although usually an exacerbation of previously extant tumors is seen. The association of a glomus tumor with neurofibroma is interesting. Masson, Slepian¹⁰⁴ and others have described unmyelinated nerve fibers in the glomus tumor and called it a "neuromyo-arterial glomus." Histologically, therefore, it is related to neurofibroma, and its clinical association may be more common than is generally believed.

CASE 2—O E, a physician aged 31, has had numerous nodules on both upper and lower extremities since the age of 10 years. Histologic examination in 1934 showed the characteristic picture of Recklinghausen's disease. In 1937 these nodules became extremely painful, and the patient entered Beth Israel Hospital where a paravertebral block was performed, with 33 per cent alcohol in 1.5 per cent procaine hydrochloride. The patient was discharged, with great relief of subjective symptoms.

This condition illustrates molluscum fibrosum also. In addition, the uncommon feature of painful nodules, after many years without symptoms, is unusual. The relief caused by the injection of alcohol and the nerve block suggests a mode of therapy in cases in which the condition becomes painful.

CASE 3—S W, a white woman aged 65, had had a small nodule in the scapular region when she was 35. The nodule was removed but recurred when she was 50 and became progressively larger, until at the age of 65 she entered the hospital to have it excised. The nodule was hard, rubbery and ovoid. It was movable laterally but not along the course of the nerve. Microscopic examination disclosed a neurinoma.

The occurrence of a single tumor (cutaneous nodule) and its recurrence after surgical removal are the features that mark this case.

CASE 4—D B, a boy aged 12 years, entered the hospital with a history of headaches for six years and abdominal pain and pigmentation for six months. His father had pigmented spots and numerous nodules about the face. The patient's younger sister, aged 5 years, also had three large pigmented spots on the abdomen. The patient was normal mentally. In the past six years he had headaches occurring almost every day and lasting several hours. The results of examinations of the eyes and ears were negative. Six months before admission the child had had an attack of acute abdominal pain, with vomiting. After the attack the child was weak, lethargic and dizzy. Five days before admission, he displayed numerous irregular areas of brownish pigmentation. In addition, a few pea-sized nodules in the left groin and left infraclavicular area were noted. Laboratory examinations, including roentgenograms of the bones, dextrose tolerance tests and chemical examination of the blood, gave negative results. Histologic examination of the left infraclavicular node revealed neurofibroma. He was discharged, but with no explanation for his abdominal attack.

104 Slepian, A. H. Glomus Tumor. Report of Two Cases with Histologic Observations, *Arch. Dermat. & Syph.* 36: 77-84 (July) 1937.

The possibility of an internal neurofibromatosis is to be kept in mind in this case. The headaches are suggestive of intracranial lesions or of acoustic neuroma, especially in view of the associated vertigo. Of course the possibility of subsiding appendicitis should not be overlooked.

CASE 5—M T, a white man aged 25, with a history of mental retardation and macrocephaly since childhood, had had pigmentation and small brownish papules on the skin since birth. The mother had had similar cutaneous lesions and had died of a tumor of the breast. The patient entered the hospital complaining of diplopia, blurred vision and severe burning pain in the right wrist and fingers. An exploratory craniotomy was performed, and a small amount of cortical tissue was removed for study. The pathologic impression was tuberous sclerosis. The cutaneous lesion represented the "fruste" type of neurofibromatosis.

This case is illustrative of the abortive type of neurofibromatosis. The association of mental retardation, the family history and the presence of macrocephaly are not unusual. The possible presence of tuberous sclerosis is again confirmatory of previously noted clinical associations.

CASE 6—H G, a boy aged 9 years, with numerous large and small light and dark brown macules over the entire body, was mentally retarded, and an encephalogram revealed internal hydrocephalus. In addition, the presence of obesity and hypoplastic genitalia led to a diagnosis of Frohlich's syndrome.

The presence of pigmentation, mental retardation and hydrocephalus is not uncommon. The presence of Frohlich's syndrome is again suggestive of the associated glandular dystrophy so frequently noted.

CASE 7—F D, a woman aged 69, with brownish macular areas on her face and most of her body, was acromegalic. Decided hypotonia of the digits, as well as osteoporosis on roentgen ray examination, suggested a diagnosis of Recklinghausen's disease of the bones (*ostitis fibrosa cystica*). This was further confirmed by a hypercalcemia, with decreased blood phosphorus and elevated phosphatase. In addition, the patient had bilateral renal calculi, further stigma of hyperparathyroidism.

The coexistence of both Recklinghausen's diseases is of interest, especially in view of the theories presented earlier in this report. The additional involvement of the pituitary gland and the pluriglandular nature of Recklinghausen's disease are again emphasized. It is not a disease of one but of many organs.

CONCLUSIONS

- 1 There is definite hereditary transmission of Recklinghausen's disease as a dominant genetic characteristic.

- 2 The origin of the tumors is mesodermal, from the connective tissue sheath of nerves (perineurium).

3 The use of a more detailed cutaneous classification is suggested. The presence of pigmentation without tumor formation is of frequent occurrence and is a definite phase of the disease.

4 Besides the cutaneous features, there are frequently associated motor, skeletal, sensory and mental disturbances.

5 The great majority of patients would show definite signs of glandular aberration if they were carefully examined for these abnormalities.

6 A syndrome with so great a multiplicity of symptoms should not be designated by a term describing but one of its phases. At the present level of knowledge the most comprehensive title is still Recklinghausen's disease.

2 East Fifty-Fourth Street

OCCUPATIONAL DERMATITIS DUE TO MINT

REPORT OF TWO CASES

WILEY MITCHELL SAMS, M D

MIAMI, FLA

The literature on contact dermatitis is extensive, and hundreds of different agents have been found responsible, yet I have been unable to find any reports on mint as a cause. Some time ago when I was discussing this subject with Dr Otto Foerster, he recalled having observed a patient with cheilitis caused by a mint-flavored chewing gum. This is the only instance I have found in which mint has been incriminated as a factor in producing a cutaneous eruption. Although physicians are now familiar with the manifestations and with many of the causes of this type of dermatitis, it is the inability at times to determine the exciting agent which leads to failure in treatment. I therefore wish to present 2 cases which have come to my attention.

REPORT OF CASES

CASE 1—K. H., a bartender at Miami Beach presented a dermatitis which began in the spring of 1934. He used various local applications without any benefit until he returned North, at which time the condition involuted spontaneously. He had been employed for many years in a similar capacity in Chicago and had never experienced any difficulty with his hands. He had no trouble during the summer, but when he returned to Florida in December he immediately began to have itching and burning about the fingers, associated with the appearance of fissures and peeling. Occasionally some small blisters occurred along the edge of the index finger and thumb of both hands. The condition persisted and continued to give him difficulty until it became so severe by February that he was unable to work. Examination at that time showed that the eruption was more extensive; it not only involved the thumb and the index and second fingers of both hands, but extended over the dorsa of the hands and onto the wrists. There were deep fissures at the finger tips, which from time to time bled, and the appearance of his hands was such that he had been unable to work for several days at a time.

A detailed history disclosed nothing suggestive, but it was found that in his occupation of mixing drinks, he handled many different fruits, liquors and fruit juices. Patch tests were carried out with all the materials which he handled in the course of his work, including limes, lemons, oranges, pineapple, mint, maraschino cherries, olives and the metal of the cocktail shaker, and only one positive result was obtained. This was with mint. There were no other reactions, even to the peel of orange, lemon and lime.

With this information at hand, he was instructed not to handle or to make any drink containing mint and not to handle the glassware in which mint had been served. His recovery began immediately, and in three weeks the hands were entirely clear. Since then he has had only one relapse. He was engaged to work

at a private party, and drinks containing mint were ordered. Even though he did not handle the mint, he was sufficiently exposed by handling the glasses and had a mild flare-up. At the time of writing three years has elapsed since his recovery.

CASE 2—R. F., a bartender at Miami Beach, had followed this occupation for approximately ten years with no previous difficulty. This was his first season in Florida, and he was free of trouble until March. About four or five days before he presented himself for examination, he noticed an eruption on both hands, which caused intense itching. Small, deep-seated blisters would break out along the edges of the fingers and in the palms. He reported slight difficulty for more than a month, and the trouble had been much more severe in the five days previous to his visit to me. The distribution along the thumb and index finger of both hands and his occupation at once suggested contact dermatitis. The results of patch tests with materials he usually handled were again negative, except with mint and orange peel. Since the oils from orange, lime and lemon peel have been reported¹ as constantly causing cutaneous reactions (primary irritants), they were not considered particularly significant. The reaction to mint was strongly positive. He was advised to avoid it completely. He did this and the eruption disappeared within less than a week and has not recurred. At the time of writing one year and two months has elapsed since his recovery.

These cases fulfil the usual criteria for contact dermatitis and are examples of epidermal sensitivity. The question which immediately presented itself, however, is why should a person (case 1) have an occupational dermatitis when working in Florida and yet have no difficulty in Chicago, although doing exactly the same work? The obvious answer is that there must be some difference in the mint used in the two localities. I had previously made the observation that the locally grown mint was a different species, but considerable difficulty was encountered in identifying the plant. The local gardeners and bartenders referred to it as "horse mint." It is propagated by root stock, and since it does not bloom, at least in this climate, much trouble was encountered in determining the species. It was learned that it had been introduced into Florida from Nassau, and it was finally identified as *Mentha citrata*, a plant native to Europe. Apparently the eczematizing properties of this plant are more marked than those of native mint (*Mentha vera*), since both of my patients are able to handle the northern mint without any difficulty.

Tests were conducted to determine the frequency with which sensitivity to *Mentha citrata* occurs. Both mint leaves and the ether-soluble fraction were used. Patch tests were made on 18 subjects with the leaf of the plant, 5 positive reactions to patch tests were obtained. An extract was made by adding one part of the residue, after evaporation of the ether, to three parts of expressed oil of almond. Forty-eight hours after the use of this preparation there were 7 positive reactions,

1 Schwartz, L. Cutaneous Hazards in the Citrus Fruit Industry, Arch Dermat & Syph 37 646 (April) 1932

1 of which was strongly positive, with large vesicles. Three of the 7 subjects who had positive reactions have recently had contact dermatitis from other agents. The extract produced reactions of greater intensity than the leaf itself, and a more dilute preparation might have been used.

Since mixed drinks are an American creation and this type of mint is used only in a restricted area, it is not to be expected that many cases of mint dermatitis will occur. With the possible exception of bartenders, few persons have any occasion to handle the plant, except infrequently. If widely used, it would no doubt be a frequent cause of contact dermatitis.

SUMMARY

An occupational dermatitis due to mint in 2 bartenders is reported. Patch tests indicate *Mentha citrata* to be a potential source of contact dermatitis.

BLOOD IODINE OF PATIENTS WITH ACNE VULGARIS

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AND

RICHARD EMMET, M.D.

NEW YORK

For some time it has been the impression of dermatologists that iodides and bromides have a tendency to cause exacerbations of acne as well as to produce acneform eruptions. While there seems to be little doubt as to the latter, acneform eruptions having become generally recognized as a complication of the ingestion of iodides and bromides, the question of their effect on acne was not so definite. We therefore undertook a quantitative study of the iodine content in the blood of persons with acne to see if there was an actual difference from the normal. A series of 58 patients was collected, consisting of 45 with acne and 13 who had miscellaneous dermatoses. In addition, Dr. Maurice Bruger placed at our disposal the values for 22 normal subjects.

There were 25 males and 33 females in our group. The extremes of range in iodine content of the blood varied from 2.67 to 17.1 micrograms per hundred cubic centimeters, the average being 6.08 and the mean, 5.7.

No effort was made to ascertain the diet of these patients at the time the test was made, nor in the case of female patients did we take the blood at any particular point in the menstrual cycle.

The relation of age to the iodine content of the blood is shown in the following tabulation:

| Age in Years | Number of Patients | Average Iodine Content of Blood
Micrograms per 100 Cc |
|--------------|--------------------|--|
| 0 to 10 | 0 | |
| 11 to 15 | 4 | 6.25 |
| 16 to 20 | 22 | 5.75 |
| 21 to 30 | 26 | 6.34 |
| Over 30 | 6 | 5.57 |

The 45 patients with acne were classified according to the severity of the condition, and the relation of the iodine content of the blood to the severity is shown in the following tabulation:

| Severity of the Condition | Number of Patients | Average Iodine Content of Blood
Micrograms per 100 Cc |
|---------------------------|--------------------|--|
| Mild | 18 | 6.25 |
| Moderate | 20 | 5.56 |
| Severe | 7 | 5.75 |
| Total | 45 | 5.975 |

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital

The remaining 13 patients had the following dermatoses. neuro-dermatitis, 2 patients, dermatophytosis and bacterid, 2, psoriasis, 2, pityriasis rosea, 1; eczema, 4, pruritus, 1, and occupational keratosis, 1. An average of 6.42 micrograms of iodine per hundred cubic centimeters of blood was found.

A definite difference was noted between the results in males and those in females, as shown in the following tabulation.

| Sex | Number of Patients | Range in Iodine Content of Blood, Micrograms per 100 Cc | Average Iodine Content of Blood, Micrograms per 100 Cc |
|--------|--------------------|---|--|
| Male | 25 | 2.67 to 7.49 | 5.3 |
| Female | 33 | 3.5 to 17.1 | 6.65 |
| Total | 58 | 2.67 to 17.1
(Mean 5.7) | 6.08 |

We have pointed out the difference in the values for males and females, but we do not believe that it is of any particular significance.

While there seem to be cases in which clinically there is no question that acne was made worse by the ingestion of iodides or bromides, our failure to find appreciable differences in the normal iodine content of the blood in these cases leads us to suspect either that there is a qualitative difference (sensitivity) rather than a quantitative one, or that the iodides are possibly being stored in the tissues rather than in the blood stream.

It has been found by Dr. Bruger that iodine is excreted in the urine and in the saliva and that there is a definite correlation between this excretion and the blood iodine level. Unquestionably the iodine is not stored in the blood.

We are now engaged in the study of iodine in cutaneous tissue, to determine whether the skin of patients with acne vulgaris contains more iodine than normal skin.

SUMMARY AND CONCLUSIONS

A series of 58 patients was studied from the standpoint of the iodine content of the blood.

Forty-five patients suffered from acne vulgaris. Thirteen patients had miscellaneous cutaneous diseases and were used as controls. Twenty-two additional, apparently normal persons, not included in the aforementioned group of 58, were also used as controls.

In the control groups of patients, whose blood iodine was apparently normal, the average value was approximately 6 micrograms per hundred cubic centimeters. The average iodine content of the blood of the patients with acne vulgaris was 5.975 micrograms, which was approximately within the normal range.

A slight difference was noted between the iodine content of the blood of males and that of females, the values for the males averaging 5.3 micrograms per hundred cubic centimeters and those for the females, 6.65 micrograms.

Differences in the iodine content of the blood of patients in various age groups were recorded.

The failure to find a higher blood iodine content in patients with acne vulgaris than in "normal" persons possibly indicates that (1) the role, if any, played by iodine may be qualitative or (2) the iodine may, in patients with this disease, be stored in the cutaneous tissues.

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FIXED ERUPTION WITH AN EXTRACUTANEOUS MANIFESTATION DUE TO MAPHARSEN

REPORT OF A CASE

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A little known but highly interesting feature of fixed effects is the occurrence of extracutaneous manifestations, appearing alone or in association with a "fixed" eruption. These manifestations consist of the recurrence in situ of pains, motor or sensory disturbances, swelling, congestion and other symptoms, in tissues other than the skin or the mucous membrane. Jadassohn, Naegeli, Milian, Bagues and others¹ observed such reactions after the repeated use of the arsphenamines, of bismuth and of mercury. Jadassohn^{1a} was the first to include these manifestations in the category of fixed effects. A detailed discussion of these reactions is contained in the excellent report by Abramowitz and Noun,² from which I have drawn freely.

The literature is rapidly becoming voluminous with reports of the value of mapharsen as an antisyphilitic agent and of its toxic effects. Those who have had experience with the drug³ unanimously agree that

From the Department of Dermatology and Syphilology, New York University College of Medicine, and the Dermatologic Service of Bellevue Hospital, service of Dr. Edward R. Maloney.

1 (a) Jadassohn, J. Zur Kasuistik der Arzneischädigungen (Salvarsan, Quecksilber, Wismut), besonders über extracutane fixe Nebenwirkungen, *Med Klin* 21:362, 1925. (b) Naegeli, O. Ueber fixe Arzneiexantheme, *Klin Wchnschr* 6:25 (Jan 1), 73 (Jan 8) 1927. (c) Milian, G. La conjonctivite arsenicale, *Paris méd* 2:303 (Oct 15) 1921. (d) Bagues, M. Crises nitritoïdes localisées, *Bull Soc franç de dermat et syph* 28:244 (May 17) 1921.

2 Abramowitz, E. W., and Noun, M. H. Fixed Drug Eruptions, *Arch Dermat & Syph* 35:875 (May) 1937.

3 (a) Tatum, A. L., and Cooper, G. A. An Experimental Study of Mapharsen as an Antisyphilitic Agent, *J Pharmacol & Exper Therap* 50:198 (Feb) 1934. (b) Foerster, O. H., and others. Mapharsen in the Treatment of Syphilis. A Preliminary Report, *Arch Dermat & Syph* 32:868 (Dec.) 1935. (c) Wile, U. J., in discussion on Foerster and others, p. 890. (d) Gruhzt, O. M., and others. Mapharsen in the Mass Treatment of Syphilis in a Clinic for Venereal Diseases, *Arch Dermat & Syph* 34:432 (Sept) 1936. (e) Wieder, L. M., and others. Mapharsen in the Treatment of Syphilis. Further Experiences, *ibid* 35:402 (March) 1937. (f) Maloney, E. R., in discussion on Wieder and others, p. 597. (g) Cole, H. N., and Palmer, R. B. Mapharsen in the Treatment of Syphilis, *Arch*

(Footnote continued on next page)

it is less toxic than the arsphenamines, the commonest reactions being of the immediate and the mild gastrointestinal type

Although fixed eruptions from mapharsen have been reported by Astrachan,⁴ Vero,⁵ Chargin and others³¹ and Abramowitz,² I have been unable to find a report of a proved extracutaneous manifestation due to this drug. In listing reactions from 75,589 injections of mapharsen administered to 4,841 patients, Gruhzt and others^{3a} found that 0.9 per cent complained of toothache or of pain in the jaws. The authors, however, did not state whether these symptoms recurred on further administration of the drug. Foerster and others,^{3b} in observing a group of 233 patients to whom 4,666 injections were given, noted mild lacrimation and from slight to profuse salivation in 4 patients. These reactions followed only the first injection. The same authors observed abdominal pain of moderate severity after the first injection in 2 cases, in 1 of which it recurred severely after the second injection. None of these cases could be regarded as an instance of a fixed extracutaneous effect, except possibly the one with the recurrent abdominal pain after the second injection. Astrachan^{4c} studied 5 patients with fixed eruptions, 2 of whom complained that after each injection of mapharsen they suffered from headaches, "soreness" of both eyes and swelling and itching of the eyelids. When seen five days after an injection of mapharsen, 1 patient had a slight erythema of one eyelid and the other only a moderate conjunctivitis of both eyes. Readministration of mapharsen resulted in the same subjective and objective symptoms. The recurrent headaches and "soreness" of both eyes suggest the possibility of a fixed extracutaneous manifestation.

Dermat & Syph **36** 561 (Sept.) 1937 (*h*) Cornell, V. A., and Astrachan, G. D. Mapharsen in the Treatment of Congenital Syphilis, *ibid* **38** 943 (Dec.) 1938 (*i*) Chargin, L., and others. Mapharsen in the Treatment of Early Syphilis, *ibid* **40** 208 (Aug.) 1939 (*j*) Kulchar, G., and Barnett, C. Mapharsen in the Treatment of Early Syphilis, *Am J Syph, Gonorr & Ven Dis* **20** 482 (Sept.) 1936 (*k*) Astrachan, D. G. Mapharsen in Antisyphilitic Therapy, *ibid* **21** 81 (Jan.) 1937 (*l*) Schmidt, L. E., and Taylor, G. G. The Treatment of Syphilis with Mapharsen, *ibid* **21** 402 (July) 1937 (*m*) Marshall, J. W. The Treatment of Syphilis with Mapharsen, *ibid* **21** 645 (Nov.) 1937 (*n*) Astrachan, G. D., and Wise, F. Further Experiences with Mapharsen. Its Use in Latent Syphilis, *ibid* **22** 470 (July) 1938 (*o*) Miller, H., and others. Mapharsen. Its Use in the Treatment of Syphilis, *California & West Med* **45** 321 (Oct.) 1936 (*p*) Parsons, R. P. Mapharsen in the Treatment of Early Syphilis, *U S Nav M Bull* **35** 207 (April) 1937 (*q*) Peterson, S. C. The Use of Mapharsen in the Treatment of Syphilis, *Canad M A J* **36** 172 (Feb.) 1937

4 (*a*) Astrachan^{3k} (*b*) Astrachan and Wise³ⁿ (*c*) Astrachan, G. D., and Sharp, E. A. The Value of Administration of Liver in Patient Intolerant to Arsenicals, *J Invest Dermat* **1** 427 (Dec.) 1938

5 Vero, F. Fixed Eruptions Due to Arsenic. Report of a Case, *Arch Dermat & Syph* **35** 307 (Feb.) 1937

The belief that I have encountered the first proved case of an extracutaneous effect from mapharsen prompted me to submit a report

REPORT OF CASE

B L., a white woman aged 22, was first seen by me on April 12, 1939. She stated that in October 1933, because of a number of indefinite symptoms, a physician performed a Wassermann test of her blood and found the reaction to be 4 plus. She was not aware of primary or secondary lesions but said she had had intercourse with a man who was receiving "arm injections." Antisyphilitic treatment was instituted immediately, and during the following three months she received twenty injections of neoarsphenamine and an equal number of injections of a bismuth preparation, with no ill effects.

From then until the time I saw her she received a regular treatment with neoarsphenamine and bismuth. The Wassermann reaction of the blood was negative on a few occasions. Recently, injections of neoarsphenamine had produced moderately severe reactions including gastrointestinal upsets, chills and fever and a scaly eruption on different parts of the body lasting for a few days. Further administration of arsenicals was considered dangerous.

From 1934 to 1937 the patient had a few attacks of dermatitis, mainly on the buttocks and thighs, that were considered to be due to a sensitivity to silk underwear. About two years before she consulted me she underwent a successful "cure" for drug addiction (heroin, diacetyl morphine). She had not taken the drug since. She frequently took sedatives of the barbituric acid group. No other drugs had been ingested.

Physical examination revealed an essentially normal condition, except for moderate pyorrhea. A urinalysis and a blood count showed no abnormalities. The Wassermann reaction of the blood was 4 plus. The patient refused to allow an examination of the spinal fluid.

After some dental care for the pyorrhea, she was given six injections of bismuth subsalicylate in oil (0.1 Gm. per cubic centimeter) in doses of 15 cc. at five to seven day intervals. There was no evidence of intolerance to this medication. I then decided to try an arsenical and administered 15 mg. of mapharsen intravenously. Ten to twenty seconds after the injection the patient complained of a severe, sharp pain in the upper jaw. The pain lasted five to ten minutes, during most of which time she held her hand to the mouth. After the pain in the jaw subsided she complained of an itch in both palms and in the left big toe. The pruritus was so intense that she began rubbing both hands vigorously and then removed the left shoe and rubbed the big toe. Examination revealed irregularly roundish, nickel-sized to quarter-sized flat erythematous plaques on both palms, on the dorsal aspect of the web between the thumb and the index finger of the right hand, on the flexor aspects of the lower third of both forearms and on the plantar aspect of the left big toe. There was no visible change in the gums while the pain lasted or after it had subsided. When the patient was seen three days later the eruption had disappeared. There was no residual pigmentation.

The patient was reluctant to receive further arsenical therapy, but a month later she consented, at which time 10 mg. of mapharsen was administered. Reactions followed, identical both in sequence and in duration but somewhat less intense. Realizing that the reaction was more annoying than serious I administered a third injection of mapharsen (20 mg.) three weeks later. The reaction recurred in all its phases, being somewhat more intense than the previous reactions. The intolerance seemed to be in proportion to the amount of mapharsen administered.

Since no other ill effects resulted, mapharsen medication was continued in doses of 20 mg at weekly intervals. So far the patient has received six injections, each one having been followed by the same sequence of events, the reactions, however, have been progressively milder (desensitization).

Experimental Data—During a period when the patient was free from any evidence of the fixed exanthem, 6 grains (0.389 Gm) of sodium amytal (sodium isoamylethylbarbiturate) and 10 grains (0.648 Gm) of soluble barbitol U S P (sodium barbital, sodium diethylbarbiturate) were ingested on successive days. No reaction of any kind followed. A subcutaneous injection of morphine sulfate $\frac{1}{4}$ grain (0.016 Gm) with atropine sulfate $\frac{1}{60}$ grain (0.0012 Gm) fifteen minutes before an intravenous injection of mapharsen not only diminished the pain in the jaw but also altered the rest of the reaction, the erythematous patches appeared faintly one hour later and lasted for only a few hours.

An intravenous injection of 0.1 Gm of neoarsphenamine produced a moderately severe reaction. Three to five hours after the injection the patient complained of malaise, nausea and slight chill and fever. Twenty-four to thirty-six hours later, small scaly patches (eczematous) appeared on most of the previously involved areas and on parts of the trunk and hips. The pain in the jaw did not appear. The eruption disappeared after ten days, leaving no pigmentation.

Patch tests with an aqueous solution of mapharsen and neoarsphenamine (0.04 Gm of mapharsen in 10 cc of water, 0.3 Gm of neoarsphenamine in 10 cc of water) gave negative results both on a normal and on a previously involved area. Intradermal tests with injections of 0.1 cc of each solution both in a previously affected area and in normal skin produced an immediate (traumatic) blotch of erythema which disappeared within two to three hours. The reaction in the previously involved area was not greater than in the normal skin.

I intended to perform further studies, but the patient refused to cooperate.

COMMENT

In the case just reported both the eruption and the pain in the upper jaw were undoubtedly instances of fixed effects due to mapharsen. This is proved by the crucial test that the reactions recurred in identical manner after each of the six injections of mapharsen and did not occur when the drug was withheld. The fact that the severity of the reactions was in proportion to the dose of mapharsen administered may be cited as additional evidence incriminating the drug. Final proof is the fact that the reactions failed to appear after a test ingestion of sodium amytal and soluble barbitol U S P (drugs which the patient had been taking frequently and which are known to produce fixed eruptions⁶) and also

6 (a) Wise, F., and Parkhurst, H. J. Drug Eruptions from the Clinical Aspect with Special Reference to the Recent Medicaments, *Arch Dermat & Syph* 6: 542 (Nov.) 1922. (b) Goldenberg, H., and Rosen, I. Skin Manifestations Seen in a General Hospital, *ibid* 14: 693 (Dec.) 1926. (c) Fowlkes, R. W. Drug Eruptions, *Virginia M. Monthly* 55: 28 (April) 1928. (d) Loveman, A. B. Experimental Aspect of Fixed Eruptions Due to Allurate, a Compound of Allonal, *J. A. M. A.* 102: 97 (Jan. 13) 1934. (e) Meredith, F. L. Reactions to Certain Barbitol Derivatives, *ibid* 102: 2099 (June 23) 1934. (f) Ormsby, O. S. A Practical Treatise on Diseases of the Skin, Philadelphia, Lea & Febiger, 1934, p. 180. (g) Abramowitz and Noun.²

after a subcutaneous injection of morphine sulfate with atropine sulfate. The latter two drugs administered fifteen minutes before an injection of mapharsen seemed to diminish the reactions.

The reaction elicited by neoarsphenamine in this case was in many respects different from that produced by the mapharsen. It is particularly noteworthy that the fixed effect of localized pain in the upper jaw was absent after the exposure to neoarsphenamine. However, the fact that the patient's skin was hypersensitive both to neoarsphenamine and to mapharsen was apparent. The possible relationship between the hypersensitivities to these two arsenicals as well as the possible causes of the differences in the cutaneous responses to the two drugs cannot be decided on the basis of the evidence presented. Nevertheless, the possibility of group reaction to both arsenicals must be borne in mind, even though the forms of reaction were somewhat different.

It is not certain whether the reaction to neoarsphenamine was of the purely fixed type or of a type which might lead to a more serious form of dermatitis on further exposure to this drug. For this reason it might be unwise to administer further treatment with neoarsphenamine. On the other hand, the cutaneous reaction to mapharsen was of fixed type and permitted the conclusion that further administration of mapharsen would be followed by reactions inclined to be more disagreeable than serious. For this reason careful administration of progressively larger doses of mapharsen does not seem to be contraindicated in this case.

The previous pyorrhea may account for the localization of the pain to the upper jaw. Naegeli^{1b} observed fixed exanthems at the site of insect bites, of a healed zoster and of a previous cellulitis. Schreiber⁷ reported the appearance of such lesions at the site of old cicatrices from burns.

SUMMARY

A case of fixed eruption with an extracutaneous manifestation due to mapharsen is reported. The eruption, which was of the erythematous type, appeared five to ten minutes after an injection and disappeared within three days, leaving no pigmentation. The extracutaneous effect consisted of severe, sharp pain in the upper jaw that appeared ten to twenty seconds after an injection and lasted five to ten minutes. Both effects recurred in identical manner after each of six injections of mapharsen in doses of 10 to 20 mg. No other ill effects occurred.

The patient was known to have intolerance to neoarsphenamine. An intravenous injection of 0.1 Gm of this drug produced a different reaction, including some systemic disturbance and a scaly (eczematous)

⁷ Schreiber. Fixes Wismutexanthen, *Dermat. Wchnschr.* 93:1642 (Oct 17) 1931.

dermatosis in the "fixed" areas and other parts of the cutaneous surface. The eruption disappeared after ten days, leaving no pigmentation. The pain in the jaw did not appear in this reaction.

Patch and intradermal tests with mapharsen and neoarsphenamine gave negative results in both the normal and the previously affected skin.

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ERYTHEMA ANNULARE RHEUMATICUM (LEHNDORFF-LEINER)

REPORT OF A CASE

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AND

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PHILADELPHIA

Cutaneous manifestations of rheumatic genesis have been known for many years. They have been brought to attention especially by internists and pediatricians, who have reported on the various ways in which the skin reacts to the infection of rheumatism and to the defense against it. In the field of dermatology only Keil¹ has during the last year directed due attention to the relation between the skin and internal medicine. Dermatologic textbooks mention, in discussion of erythema multiforme, erythema nodosum, formations of cutaneous and subcutaneous nodules and purpura, the possibility of a rheumatic genesis and the fact that in rheumatism the Libman-Sachs syndrome may occur in addition to the aforementioned dermatoses. But there is an almost complete absence of a closer differentiation of the most important group, that of erythemas. Keil classified rheumatic erythema as (1) the simple papular form and (2) the ringed form, of which there are two kinds, erythema marginatum rheumaticum and flat annular erythema. The present study is concerned with the last-mentioned form.

In 1922 Lehdorff and Leiner² described a dermatosis in children that they regarded as typical when there was a cardiac condition in a patient with acute rheumatism. It is true³ that this picture had apparently been described in the older French literature by Besnier,⁴ Rayer⁵

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1 Keil, H. The Rheumatic Erythemas. A Critical Survey, *Ann Int Med* 11:2223, 1938, The Rheumatic Subcutaneous Nodules and Simulating Lesions, *Medicine* 17:261, 1938.

2 Lehdorff, H., and Leiner, C. Erythema annulare, ein typisches Exanthem bei Endokarditis, *Ztschr f Kinderh* 32:46, 1922.

3 Grenet, H. Erythème rhumatismal (érythème marginé en plaques discoïdes de Besnier, érythème annulaire de Lehdorff et Leiner), *Bull et mém Soc méd d hôp de Paris* 52:1117, 1936.

4 Besnier, cited by Grenet³.

5 Rayer, P. F. O. *Traité théorique et pratique des maladies de la peau*, ed 2, Paris, J. B. Baillière, 1835.

and Cheadle⁶ under the name *erythème marginé en plaque discoides*, but Lehdorff and Leiner studied the dermatosis thoroughly and clarified its pathogenesis and prognosis

While only Keil seemed to be acquainted with rheumatic annular erythema from the dermatologic standpoint, there are some good English articles⁷ concerning it, which, however, do not contain any new information

According to the exposition of Lehdorff,⁸ the cutaneous manifestations are characterized by paleness, delicacy, a transitory nature and absence of local subjective symptoms. This may be the reason why the dermatosis is not well known. (Lehdorff estimated that 10 per cent of all children with rheumatic fever show it.) The first efflorescences are pale red or pale livid half-circles or rings, at most 1 to 3 mm broad, which become more distinct if the patient is allowed to remain uncovered for a while. Almost always they appear first on the trunk (chest and abdomen) and then on the lateral parts of the thorax and on the back. On the extremities the lesions appear less frequently, avoiding the extensor surfaces (in contradistinction to erythema multiforme) and appearing on the inner surfaces of the thighs. The hands and feet always remain free. In the succeeding hours and days the rings and circles become more numerous and larger and through confluence form polycyclic figures. The lesions are never papular but are on the level of the skin. The eruption is characterized by negative signs, there is never any itching, edema, hemorrhage or swelling of the follicles. The lesions disappear without scaling or pigmentation. The eruption usually lasts two to three days. At times it appears only once in the course of the rheumatic condition, and at times it recurs with each attack. The mucous membranes are never involved.

Histologic examination (Carol and van Krieken⁹) shows acute inflammation, with polymorphonuclear leukocytes in the papillary and subpapillary layers, in part, with distinct perivascular arrangement along

6 Cheadle, W. B. *The Various Manifestations of the Rheumatic State as Exemplified in Childhood and Early Life*, London, Smith, Elder & Co., 1889

7 (a) Abt, A. F. *Erythema Annulare Rheumaticum*, *Am J M Sc* **190** 824, 1935. (b) Perry, E. B. *Erythema Marginatum (Rheumaticum)*, *Arch Dis Childhood* **12** 233, 1937. (c) Wallgren, A. *Studies on Erythema Annulare Rheumaticum*, *Acta pædiat* **17** 447, 1935.

8 Lehdorff, H. (a) *Erythema annulare rheumaticum*, *Wien med Wchnschr* **80** 1449, 1930. (b) *Die Erythemkrankheiten im Kindesalter*, in von Pfaundler, M., and Schlossmann, A. *Handbuch der Kinderheilkunde*, Leipzig, F. C. W. Vogel, 1935, vol. 10, p. 584.

9 Carol, W. L. L., and van Krieken, J. A. *Zur Histopathologie des Erythema annulare von Lehdorff und Leiner*, *Acta pædiat* **17** 372, 1935.

the dilated vessels. The eruption occurs usually in children. However, it may occur, though rarely, in young adults (Lehndorff⁸ and Keil¹).

This form of annular erythema is characteristic of "rheumatic infection" (We wish to add that other forms of erythema annulare are known to dermatologists, which, however, are differentiated from the aforementioned type of differences in course and by the absence of any connection with cardiac manifestations). Erythema as described by Lehndorff and Leiner is never observed with malignant, septic or ulcerative endocarditis or with the endocarditides that appear in the wake of various infectious diseases. As Lehndorff especially has pointed out, it apparently never appears with the "rheumatoid" articular conditions that occur as sequelae of such diseases as scarlet fever and sepsis. Finally, erythema annulare has no relation to the polymorphous eruptions of exudative, urticarial and purpura-like conditions described in connection with rheumatism.

Erythema as described by Lehndorff and Leiner is a manifestation of rheumatic infection and usually of that stage in which endocarditis is demonstrable or in which certain general symptoms, such as anemia, irritative cough and dyspnea, point to disease of a valve.

The diagnostic significance of annular erythema has been considered of great importance by such authors as Lehndorff,⁸ Leichtentritt,¹⁰ Keil,¹ Abt^{7a} and Schmidek.¹¹ We also, in the course of years and on the basis of 4 cases, have become convinced that one who can recognize the eruption can diagnose the presence of rheumatic heart disease on the mere appearance of the cutaneous lesion. The characteristic eruption has the same importance as do the nodules of rheumatismus nodosus, with which it is sometimes¹² associated (as in 2 of our own cases).

Views as to the prognosis of the condition are divided. Lehndorff, Knoepfelmacher and others, at least in their first communications, considered the prognosis unfavorable, in the sense that the process slowly leads to damage of the circulation, cardiac insufficiency and finally death. Other authors, such as Leichtentritt, have been more optimistic.

Few opinions have been expressed up to the present concerning the pathogenesis. We are of the opinion that three possible origins are to be considered: metastatic-bacterial, toxic and allergic.

It is true that Reitter and Lowenstein¹³ have reported from the Knoepfelmacher clinic in Vienna that they could cultivate tubercle

10 Leichtentritt, B. Die rheumatische Infektion im Kindesalter, *Ergebn d inn Med u Kinderh* **37**:62, 1930.

11 Schmidek, B. Ein Fall von Erythema annulare, *Med Klin* **32** 1048, 1936.

12 Lehndorff^{8a} Perry^{7b}

13 Reitter, C, and Lowenstein, E. Ueber den pathogenetischen Zusammenhang des akuten Gelenksrheumatismus mit der Tuberkelbazillämie, *Wien klin Wchnschr* **45**:293, 1932.

bacilli from the blood of children with erythema annulare, but, as is known, the observations of Lowenstein are not generally accepted. The transitory nature and the often month long uninterrupted relapses

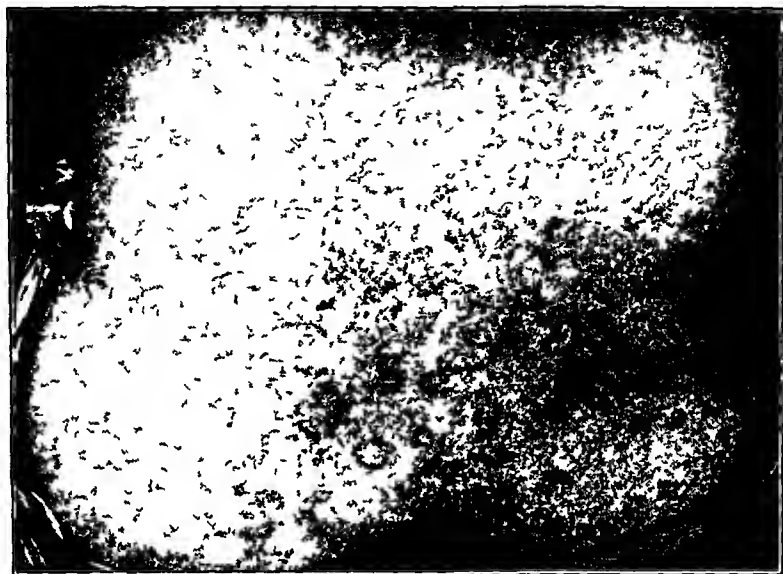


Fig 1—Type of distribution of the lesions in erythema annulare rheumaticum (Lehndorff-Leiner)



Fig 2—Detail of the annular configuration

are not in accord with a bacterial genesis of the erythema. Nor do toxic conditions last so long as a rule, and they do not have the transitory character of the eruption in question. We, on the contrary, adhere

rather to the supposition¹⁴ that a cutaneous allergy is likely to be the basis of the condition. In favor of this opinion are not only the ephemeral nature of the cutaneous lesions but the fact that our patient showed an excessive hypersensitivity to Witte's peptone, such as, in our experience, is found only in patients with cutaneous allergy.

REPORT OF CASE

H W, at the age of 7 years, had an attack of grip, followed by decided articular swellings and high fever. A disseminated ephemeral eruption of bizarre form then appeared. In addition, there appeared over almost all the joints and the scalp painful millet seed-sized to bean-sized nodules, which were freely movable on the underlying tissues. Over the heart was heard a loud, rough systolic murmur, loudest at the base, and an accentuated second pulmonic sound. The pain and swelling of the joints disappeared in three months. Subsequently the patient presented the same manifestations and was hospitalized three times. In the last few years the pains in the joints have been less frequent and milder, but the erythema has always recurred. Some weeks before the last admission the patient had severe angina, at which time severe pains in the joints again appeared. For this reason the tonsils were removed. After the operation there was a recurrence of the exanthem. At the same time the so-called rheumatic nodules again appeared. They were freely movable, painful and about the size of beans and appeared especially over the affected joints and on the scalp. The exanthem was formed partly of circles and partly of open rings (figs 1 and 2), which were a delicate bluish gray. Worthy of notice is the transitory course, the cutaneous manifestations after four hours having either disappeared or assumed new forms by confluence.

Physical examination showed a distinct systolic murmur, loudest at Erb's point, and an accentuated secondary pulmonic sound. A roentgenogram showed an enlargement of the left ventricle, which is a sign of a compensated mitral insufficiency. Morphologic examination of the blood showed a distinct shift to the left, with a slight lymphocytosis, the lymphocytes being increased considerably in size.

| | | Differential Count | |
|-------------------|---------------------|--------------------------------|-------------|
| Erythrocyte= | 4,660,000 per cu mm | Segmented neutrophils | 48 per cent |
| Hemoglobin (Sahl) | 79 per cent | Stab neutrophils | 16 per cent |
| Color index | 0.6 | Monocytes | 4 per cent |
| Leukocytes | 4,900 per cu mm | Lymphocytes (especially large) | 32 per cent |

The sedimentation time of the blood was decidedly increased (23 mm, Westergren). The urinalysis gave normal results. During the stay in the hospital new foci of erythema appeared almost every day. The patient complained of severe pains in the joints and showed signs of an infection, in the form of exhaustion and pyrexia.

Treatment for the eruption had not been previously undertaken, principally because of the fact, no doubt, that the condition had never been treated by dermatologists but always by pediatricians, who naturally turned their attention to the internal manifestations. We tried to excite the formation of so-called

14 Bindschedler, J J. Erythema annulaire rheumatismal de Lehndorff et Leiner chez un garçonnet, Bull Soc franç de dermat et syph 43-856, 1936 Wallgren^{7c}

metaspecific antibodies (according to Urbach)¹⁵ by fever treatment with pyrifur (a nonspecific protein mixture prepared from extracts of fever-producing bacteria of nonpathogenic stocks). Actually the patient during and after the fever was free of cutaneous and articular manifestations. It was further noticed that the fever was remarkably well borne in spite of the existing endocarditis. Some days later, however, new lesions of erythema appeared. We then sought to induce the formation of metaspecific cutaneous antibodies by means of ultraviolet rays. Under this treatment the cutaneous lesions changed. On the appearance of erythema from the ultraviolet irradiation the lesions became urticarial instead of remaining at the level of the skin as before, and the patient complained of severe itching in the areas affected. Some hours later the dermatitis on the skin subjected to irradiation disappeared, and it stayed away for some days, the remainder of the body presenting annular foci of erythema. Because of this fact we gave systematic ultraviolet irradiation, the patient being thoroughly irradiated on several occasions.

It is perhaps interesting that a morphologic examination of the blood carried out at the end of treatment showed an essentially different result from the aforementioned one.

| | |
|---|------------------|
| Leukocytes | 7,600 per cu. mm |
| Segmented neutrophils | 58 per cent |
| Stab neutrophils (considerably fewer) | 6 per cent |
| Monocytes | 4 per cent |
| Lymphocytes (many smaller forms than in the previous count) | 28 per cent |

Whether the result of this metaspecific therapy will be permanent no one can say. The result is perhaps worthy of attention in view of the resistance of the condition to other forms of therapy.

SUMMARY AND CONCLUSIONS

Attention is directed to a disease picture of a rheumatic infectious genesis not well known in the dermatologic literature, the so-called erythema annulare rheumaticum of Lehdorff-Leiner.

We report a case in which the disease had an interrupted course for twelve years and was associated with subcutaneous nodules. It is one of the few cases in which such a condition has been observed in an adult.

Metaspecific treatment was tried by means of ultraviolet irradiation, in order to increase the cutaneous antibodies, which led to the result that the patient has remained free of the manifestations for a certain time. The etiopathology cannot be decided with certainty, but the transitory character of the eruptions and the high grade of cutaneous hypersensitivity to Witte's peptone are in accord with the fact that the cause of the disease is allergic and bacterial.

¹⁵ Urbach, E. *Klinik und Therapie der allergischen Krankheiten*, Vienna, Wilhelm Maudrich, 1935.

TREATMENT OF PRURITUS ANI BY TATTOOING WITH MERCURY SULFIDE

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In spite of the voluminous literature on pruritus ani, the subject remains but little understood. It has not yet been determined whether it is a symptom or a disease entity. Many observers believe that local lesions, such as polyps, hemorrhoids, fissures, fistulas, hypertrophied papillae, infected crypts of Morgagni and infected anal ducts, are important causative factors. Ault¹ emphasized the etiologic importance of infection which originates in the anal ducts and in the crypts of Morgagni. On the other hand, "Tucker and Hellwig" stated the belief that pruritus ani is caused by a chemical dermatitis. The latter is said to be due to the passage of feces containing an excess of hydrocarbons, such as skatole.

Local dermatologic conditions, such as neurodermatitis, psoriasis, eczema, seborrheic dermatitis, bacterial and fungous infections and dermatitis medicamentosa, may cause pruritus ani. Systemic diseases, such as diabetes mellitus and hepatic, renal and gastrointestinal diseases and dysfunctions, may produce pruritus ani in certain persons. Pruritus ani may also be brought about by disease of the genital organs and of the lower part of the urinary tract.² Intestinal parasites, especially *Oxyuris vermicularis*, may produce pruritus ani in children and in adults. Psychoneurosis and allergy, although their roles are little understood, are often incriminated.

From the Division of Proctology, Department of Surgery (Harold K. Tanner, Director), The Brooklyn Hospital.

1. Ault, G. W.: Recent Advances in Proctology, M. Ann. District of Columbia 6:29-38 (Feb.) 1937.

2. Tucker, C. C., and Hellwig, C. A.: Pruritus Ani, Arch. Surg. 34:929-938 (May) 1937.

3. Turell, R., and Marino, A. W. M.: The Intestinal Phase in Urologic Disease, J. Urol. 42:197-203 (Aug.) 1939.

There also is the so-called essential or idiopathic type, which is now less frequently encountered than in former years.⁴ Patients with this type should be given the benefit of exhaustive investigation by a proctologist, a dermatologist, an internist and a psychiatrist, the services of a urologist and a gynecologist also are at times essential.

Investigators who believe that anorectal disease is the principal cause of pruritus ani advocate the eradication of all lesions as the first step in therapy. This therapeutic approach will probably cure or relieve the condition in many cases, but it fails in a certain number. The good results are often of short duration. In the cases of recurrent pruritus ani following proctologic operations, it is likely that the local lesions have been incompletely removed. We believe that concomitant anorectal lesions, regardless of their etiologic importance in pruritus, should be eliminated in all cases of pruritus ani. This applies especially to the eradication of any neoplastic disease, such as polyps, and of inflammatory lesions, such as fistulas, infected crypts of Morgagni and infected anal ducts. This policy is equally applicable to dermatologic lesions and systemic diseases. However, when pruritus ani persists despite these measures, treatment should be directed to the pruritus alone.

An appraisal of the value of the therapy of pruritus ani should take into consideration the fact that over two hundred different forms of treatment have been proposed.⁵ A critical attitude, therefore, toward a newly proposed form of treatment is justified. Nevertheless, the distressing character of the lesion warrants the trial of new procedures. It is with such an attitude that we approached the investigation of the treatment of pruritus ani by tattooing with mercury sulfide.⁶ This method is not new in cutaneous therapeutics. Cattani,⁷ a Swiss dermatologist, long ago suggested the employment of tattooing with mercury sulfide for the treatment of localized chronic cutaneous lesions. He based his recommendation on the knowledge that syphilitic cutaneous lesions were never observed in the areas tattooed with mercury sulfide (cinnabar). It is of further interest to note that Carton⁸ in 1909 described the therapeutic use of tattooing by the natives of North Africa for a variety of lesions, including neuralgias.

4 Turell, R., in discussion on Sulzberger, M. B. The Effect of Tattooing with Mercury Sulfide Cinnabar on Pruritus Ani, *Arch Dermat & Syph* 40:493 (Sept.) 1939.

5 Simmons, N. J. Pruritus Ani. New Treatment, *Am J Digest Dis & Nutrition* 2:53-55 (March) 1935.

6 Hollander, E. Treatment of Pruritus Ani by Tattoo with Mercuric Sulfide, *Arch Dermat & Syph* 38:337-339 (Sept.) 1938.

7 Cattani, P. Das Tatauieren. Eine monographisch Darstellung vom psychologischen, ethnologischen, medizinischen, gerichtlich-medizinischen, biologischen, histologischen und therapeutischen Standpunkt aus, Basel, Benno Schwabe & Co., 1922.

8 Carton, cited by Cattani.⁷

TECHNIC

The armamentarium consists of an electric tattooing machine (3,000 vibrations per minute) with needle handles containing six to twenty needles in a single row and protruding 2 to 3 mm. The present day machines are still too crude and need improvement. From 8 to 15 volts is required, depending on the tension of the spring. A technical knowledge of the component parts of the machine, such as the terminals, the switchboard, the footswitch and the rheostat, is essential. The machine and the needles should be sterilized by formaldehyde vapor.

A paste of mercury sulfide in sterile distilled water is used. Infiltration anesthesia with 0.5 to 1 per cent procaine hydrochloride is preferred. In order to evaluate critically the results of this form of therapy, we decided not to employ any other type of anesthetic, particularly the oil-soluble ones which are frequently employed for the relief of pruritus ani. The perianal skin is prepared as for any anorectal procedure.

Considerable practice is required to master the technic. The handle of the machine should be held at an acute angle to the skin, and it is advanced slowly, with an even stroke. The skin should be held taut to facilitate the penetration of the needles and the mercury sulfide into the corium. Tattooing in the average case is completed in forty to sixty minutes. However, when deep folds are present the procedure is better carried out in two sittings. At times it is impossible to avoid missing small areas. These can be dealt with at a subsequent time, if necessary. The perianal skin in some cases is extremely thin and cracks easily when held taut. To deposit mercury sulfide in such skin is extremely difficult. After the completion of the treatment, the tattooed area is covered with phenolized petrolatum. Edema and tenderness may persist for about twenty-four to forty-eight hours. To relieve the edema and tenderness applications of witch hazel and hot hip baths are soothing.

RESULTS

After a fairly extensive review of the literature, no references were found to reports of systemic manifestations of the toxicity resulting from the intracutaneous deposit of mercury sulfide in normal skins by tattooing. Cutaneous reactions to mercury following tattooing have been observed, however. Ballin⁹ reported on the delayed cutaneous hypersensitivity to mercury. His patient exhibited cutaneous manifestations two years after the tattooing. Another interesting feature in his case was the fact that the patient reacted positively to patch tests with a 2 per cent ammoniated mercury ointment and with a 1:1,000 solution of mercury bichloride but failed to react to the patch and scratch tests made with mercury sulfide.

There appears to be no reported study on the toxicity resulting from the tattooing of pathologic skin with mercury sulfide. Total hematuria and transient albuminuria occurred in our case 7A six days after the posterior half of the perianal circumference was tattooed with mercury sulfide. A routine urinalysis made prior to treatment showed no abnormalities in this case. To date we have failed to observe

⁹ Ballin, D. B. Cutaneous Hypersensitivity to Mercury from Tattooing. Report of a Case, *Arch. Dermat. & Syph.* 27:292-294 (Feb.) 1933.

cutaneous sensitivity, with the possible exception of 2 instances in which a slight degree of transient scaly dermatitis occurred. This fact notwithstanding, utmost care should be exercised, since mercury sulfide under ordinary circumstances has been found to be moderately toxic¹⁰. It is known that metallic mercury and mercury compounds are absorbed readily from all surfaces. The occurrence of mercury poisoning is dependent on the depth of the deposit in the skin and on the quantity of the drug used. It should be remembered that in tattooing for the treatment of pruritus a large quantity of mercury sulfide is deposited in pathologic skin covering an area of about 50 sq. cm.

The possibility of mercury poisoning is increased when subcutaneous deposits of mercury sulfide are made. Neal¹¹ stated: "It is the consensus of medical opinion that any mercury compound brought into contact with the subcutaneous tissues will undergo a chemical change with the formation of a mercury proteinate, and in this way it will be gradually absorbed." Subcutaneous deposits may occur when the thin perianal skin cracks while being held taut.

A peculiar sensation in the perianal region which none of the patients was able to describe developed in 5 instances about two weeks after the completion of the treatment.

This paper is based on the study of 22 patients, 14 of whom were treated and followed at the Brooklyn Hospital. We have employed the procedure of tattooing with mercury sulfide in the treatment of patients with refractory pruritus and for a number of years, as shown by the illustrative case reports.

REPORT OF CASES

CASE 3—H. F., a 31 year old automobile mechanic, had had pruritus and for many years. His history included a neurectomy performed on May 16, 1932, according to the technic of Charles Ball, subcutaneous injection of alcohol and benacol (a proprietary local anesthetic said to contain paraaminobenzoyl ethanol benzoate and phenmethylol) in 1935 and a rectal operation performed in 1936.

CASE 6—C. C., a 53 year old man, an employee at another hospital, had had severe pruritus and for over five years. Because of extensive involvement, the right half of the perianal circumference was first tattooed. Two days later the pruritus of the untreated parts was so severe that one of the attending surgeons referred him to one of us (A. W. M. M.) for immediate attention. An oil-soluble anesthetic was injected subcutaneously, with instant relief. Six weeks later there was a return of the pruritus, which necessitated more treatment. The left side was then tattooed with mercury sulfide.

CASE 8—M. W., a 50 year old housewife, had had pruritus and for seven years. The right side of the perianal circumference was subject to more itching than the

10 Neal, P. A. Personal communication to the authors, Jan 11, 1939.

11 Neal, P. A. Personal communication to the authors, May 5, 1939.

left The past history included syphilis, which was adequately treated, and a rectal operation performed on May 4, 1938, when infected crypts of Morgagni were removed

CASE 10—W R, a 36 year old salesman, had psoriasis over the elbow joints and pruritus ani for twenty years A rectal operation had been performed in 1925 The family history revealed that his father, his sister, two brothers and a nephew had pruritus ani Most of them lived in different parts of the country. The left perianal circumference was tattooed with mercury sulfide, while on the right side another mercurial chemical was employed

CASE 14—M A, a 44 year old housewife, had had pruritus ani for over seventeen years There was psoriasis on other parts of the body and possibly over the anterior aspect of perianal region

CASE 2A¹²—F F, a 29 year old housewife, had had pruritus ani for nine years The past history included a rectal operation performed in 1935 and a subcutaneous injection of alcohol in 1937 Suicidal tendencies were most manifest

CASE 7A—A P, a 66 year old retired man, had had pruritus ani for over fifteen years He had had a rectal operation in 1931 and another in 1937 Examination revealed a weeping and macerated perianal skin with numerous fissures extending to the scrotum and over the buttocks and a wide area posteriorly

CASE 4A—S R, a 26 year old accountant, had had pruritus ani for eight years He was treated with the tattoo machine without medication Twenty-two days later he was tattooed with mercury sulfide for recurrent pruritus, and he has had relief to the time of writing

CASE 9—B S, a 28 year old barber, had had pruritus ani for over six years He also required tattooing with mercury sulfide within three weeks after tattooing without the use of the chemical

CASE 5—A F, a 44 year old housewife, had had pruritus ani for over five years The right half of the perianal area was tattooed with mercury sulfide She was free from pruritus for one month, but then itching again developed in the untreated area The left half of the perianal circumference was then treated like the right one but without the use of mercury sulfide However, the patient received the impression that the sides were treated alike. Except for periods of pruritus of five minutes' duration the day before the onset and the day after the cessation of the menses, she continued to be free from itching

COMMENT

The results obtained from this treatment have been so satisfactory as to justify its continuation A prolonged follow-up period will be necessary for the final evaluation of the method A correct appraisal of the result that is to be expected in an individual case can be made usually within a short time after the completion of the treatment One of us (R T) has followed 2 private patients for over nine months Our clinic patients have been followed for seven months In case 3

¹² Cases identified by number and letter are those of Dr Turell's private patients

there was a definite recurrence of pruritus of four days' duration, but it disappeared spontaneously. The patient was tattooed on Feb 2, 1939. The recurrence was noted on May 13, 1939, fourteen weeks later. In all fairness to the method of treatment, it should be added that the perineum and perianal region of this patient, an automobile mechanic, was constantly irritated by oil-laden clothes. However, the freedom from pruritus even for a short period of time was considered distinctly worth while by the patient. In case 6 a localized sensation was noted two weeks after the left half of the perianal region was tattooed with mercury sulfide. A sensation in the perianal skin, which none of the patients described precisely but which was definitely unlike the character of the original pruritus, occurred in 4 other patients, in most of them within two weeks after completion of treatment. In case 3, this eventuated in transient pruritus within fourteen weeks. In case 1A the sensation disappeared completely about a month after its appearance.

The *modus operandi* of this form of treatment is unknown. The mercury may have either an antiseptic action or a chemical effect on the cutaneous nerve supply. It is possible that the combined chemical and mechanical effects are essential. To determine whether the drug was necessary or not, 4 patients were treated with the tattoo machine but without the use of mercury sulfide. Relief from pruritus was obtained for a very short time. In all cases the recurrent pruritus disappeared after the tattooing with mercury sulfide. Cases 4A and 9 illustrate the insufficiency and the ineffectiveness of the mechanical excitations produced by the tattooing machine alone.

It is also possible that the psychic element in some cases is as important as the physical and chemical aspects. The role of the power of suggestion is illustrated by the experience with case 5. It is of interest to note that Carton⁸ could not tell whether tattooing had a direct therapeutic or psychic effect. The association of tattooing therapy with neural lesions and the possible psychic effects of this treatment on the uncivilized natives of North Africa have more than passing significance.

SUMMARY AND CONCLUSIONS

A critical analysis of the treatment of pruritus and in 22 cases by tattooing with mercury sulfide is presented. This form of treatment has been tried in instances of refractory pruritus and with satisfactory results. Old and established modes of therapy are adequate and should not be discarded until the rationale and the safety of this newer procedure is established. A less enthusiastic but a more critical attitude is still in order.

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NATURAL COLOR PHOTOGRAPHY OF THE SKIN

A NEW APPARATUS FOR PROPER ILLUMINATION

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DETROIT

In the recording and teaching of dermatology, photographs and lantern slides have always played a large part. The one drawback has always been that the delineation had to be in shades of gray instead of the natural color of the skin, whereas differentiation of diseases of the skin often depends not only on configuration but on differences in color. It is true that hand-colored photographs and lantern slides have at times been presented and that in recent years actual color photographs have been made, by the separation method, but this has represented a large degree of technical skill and a somewhat prohibitive cost.

With the introduction of kodachrome and dufay color film and its adaptation to the small camera, the factors of both cost and technical skill rapidly became less material. The difficulties in obtaining true color rendition have been in a measure solved by the manufacture of films that can be used in daylight or in artificial light, with the use either of filters or of the proper film for the illumination present.

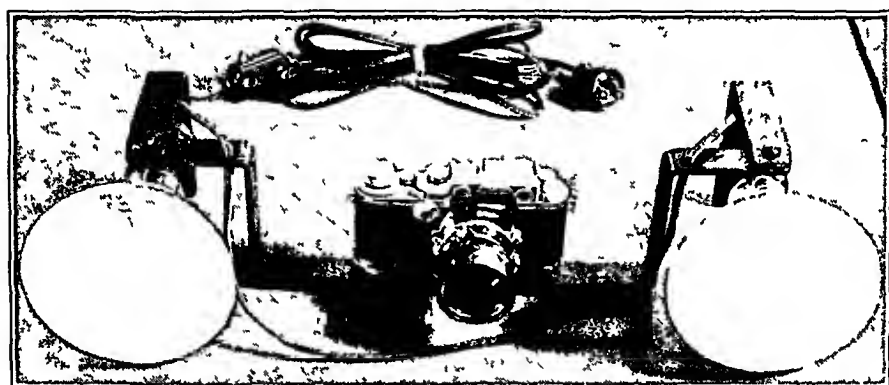
Artificial light because of its uniformity, has proved to be the best form of illumination for taking color pictures of diseases of the skin. The film for this type of light is balanced for the use of photoflood bulbs and has a comparatively high speed, allowing short exposures and small aperture lenses, with a considerable increase in depth of focus. Unfortunately the film does not have much latitude, so that the exposure must be correct to within one stop of the lens.

The prime necessity in color photography with artificial light is to have flat lighting, i. e. the subject must be equally lighted from both sides of the camera. In order to obtain this effect with a minimum amount of space and without the necessity of frequent adjustments of light and camera I have made a modification of an often used principle and devised an apparatus which may be used either in the hand, for short exposures or mounted on a tripod for longer ones. It will give essentially flat lighting for all types of dermatologic color photography.

The apparatus is made of an aluminum bar 10 inches (25 cm) long, with a $7\frac{1}{2}$ inch (19.1 cm) hole in the center for ordinary cameras and an off-center hole for Leica cameras. At each end this bar bends upward $3\frac{1}{2}$ inches (8.9 cm) and over $3\frac{1}{4}$ inches (8.3 cm) to clear the barrel of the lamps and a swivel joint attaches an "L" 4 inches (10 cm) long,

which turns down 4 inches (10 cm) At the back of the "L's" are mounted two heat-resisting sockets, each of which holds a General Electric R-2 photoflood bulb The clear space at the rear of the photoflood bulb is painted with reflecting aluminum paint Both sockets are wired together to a 10 foot (3 meter) line for 110 volts, and there is a manually operated switch in the line The entire device, with bulbs, is so balanced that it sets upright on a table, with or without the camera The camera is attached in the proper position by a tripod screw A leatherette-covered fiber case has also been devised which keeps the apparatus in position for instant use as removed from the case, with a compartment for such accessories as extra bulbs, films and flashlight bulbs

To operate, the camera is firmly attached to the apparatus, the lights are turned on and a reading is taken with the exposure meter, which



Apparatus for the proper lighting of the subject in the taking of colored photographs

*Kodachrome Exposure Guide for Type A Artificial Light Film Using
General Electric Self-Reflecting Photoflood Bulbs*

| Distance of Lamps from
Subject in Feet | Opening |
|---|---------|
| 5.5 | f8.5 |
| 4.0 | f4 |
| 2.5 | f6.3 |
| 2.0 | f7.5 |
| 1.5 | f9 |
| 1.17 | f11 |

should be, preferably, of the photoelectric type Readings differ, however, depending on the amount of light reflected from the part to be photographed An average reading can be taken if a medium gray card is held against the patient, this being more accurate than taking multiple readings and dividing the results by the number of readings

taken. The accompanying exposure chart has been devised by the trial and error method and is reasonably accurate.

It is assumed that with all of these camera apertures, the shutter speed will be one twenty-fifth to one thirtieth of a second. For light-colored subjects, stop down one-half stop. For dark-colored subjects, open up one-half stop.

It is to be remembered that photoflood lamps have a relatively short life and that after continued use the light value is lessened. Allowance in exposure must be made for this point. It is also important to remember that it takes the equivalent of one stop more for pictures of Negro skin than it does for white. Otherwise, underexposure will result.

Needless to say, cameras must be accurately focused. Reflector types of cameras or those with ground glass backs may be focused directly on the ground glass with the aid of a magnifier and thus insure a sharp focus. Cameras that have automatic range finders usually focus anywhere from 3 to 6 feet (0.9 to 1.8 meter), and it is necessary when focusing for close-ups either to have special adaptors or to use front lenses and tapes to measure the distance accurately and then depend on a table of distances for the result.

The prime object of the apparatus here presented is to provide a handy, portable method of illumination for the taking of colored photographs of cutaneous conditions.

10 Peterboro Avenue

EFFECTIVE TREATMENT OF VARICOSE ULCERS OF THE LEG

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Varicose ulcers have long been considered one of the most troublesome conditions confronting the general practitioner and to some extent even the specialist. The mass of literature on the subject, giving a variety of modes of treatment and technic as numerous as the publications themselves, shows the difficulties which the physician has to face. One of the most comprehensive contributions to the subject has been made by Nobl,¹ whose monograph so completely covers the etiology and pathology of varicose ulcers that it does not come within the scope of this paper, which is devoted to practical suggestions for effective treatment, to discuss the matter in detail again.

In order to clear up a varicose ulcer it is necessary (1) to eliminate the cause, (2) to stimulate the granulation of the ulcer and (3) to improve the circulation of the blood and the lymph.

If the ulcer is not caused by thrombophlebitis, the varicose veins must first be obliterated by the injection method. In case of thrombophlebitis, however, the injection method should under no circumstances be employed as long as active inflammatory processes are present, and even after the thrombophlebitis has subsided, caution must be exercised, since the condition is apt to flare up again easily. Those varicose veins which surround the ulcer or are in its proximity should be sclerosed first in order to restore better blood circulation to the ulcer. The artificial inflammation of the vein and occasionally of the surrounding tissue, caused by the obliteration of the vein, results in an increase of leukocytes in that tissue to the extent that they form a wall or a barrier around the ulcer.

Regarding the stimulation of granulation tissue, the following technic has been used in our clinic for the last two years after having been successfully tried in private practice for a number of years.² After

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1 Nobl, G. Der varikose Symptomenkomplex, Vienna, Urban & Schwarzenberg, 1918.

2 Isaak, L. Feinsilber zur Ulcus-cruris-Therapie, Dermat. Wchnschr. 92: 807, 1931.

protecting the surrounding skin by a thick layer of zinc oxide paste, the ulcer itself is covered with a few layers of thin genuine silver leaf, which is generally used by sign painters to paint silver letters on windows and which is available in three brands, an American, a German and a Japanese, of which we found the American to be the thickest and therefore the best. They can be purchased in any paint store. The ulcer is then covered with a thick layer of cotton and bandaged tightly. The silver leaf treatment has a double effect, the air-tight occlusion of the ulcer forming a wet chamber, a treatment formerly accomplished by adhesive strappings or a cover of lead or zinc foil,³ and having also an apparent catalyzing effect. Fresh red and healthy granulations under the silver leaf appear quickly without having a tendency to decay. The oozing of the wound decreases remarkably, and the fetid odor of the ulcer rapidly disappears. Among the ulcers I treated at the clinic was a roentgen ray ulcer occurring on the hand. It did not clear up when treated with Aloe vera leaf, but responded quickly to the treatment with silver leaf. It is important to protect the surrounding tissue with zinc oxide paste, in order to prevent maceration of the skin by the secretion of the ulcer. The cotton which has been placed on the silver leaf is used to absorb the secretion. It is understood that the ulcer must be dressed again in three to eight days, according to individual needs. If there should be much secretion a burning pain will appear and a new dressing of the ulcer is indicated. The surrounding tissue is then washed with purified petroleum benzine, ether or olive oil.

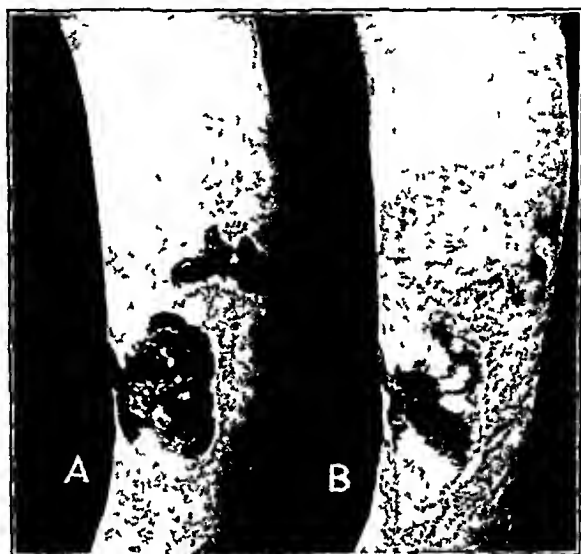
To restore blood circulation in the leg to a healthy state, one may apply zinc-gelatin bandages (Unna's boot) from the toes up to the knee. Formerly the application of these bandages was rather troublesome and wearisome, but there are now available several types of such ready-made bandages manufactured in this country, which greatly facilitate the dressing, as they are ready to use after removal from their containers. The bandage must be applied tightly in this way.

Elevate the leg for a few minutes, after local treatment of eczema or ulcer and application of padding, especially underneath the knee, so that the bandage does not cut into flesh, and along the protruding tibia, a protecting gauze bandage or stockinette is first put on to prevent sticking of the bandage to the hair. Start bandaging on the lateral side of the foot just above the toes, and then proceed under the sole and around the inner side of the foot, so that the arch is lifted properly, repeat this turn once or twice, and then bring the

3 Lang, M. Die feuchte Kammer in der Behandlung der Hautulcerationen, besonders der varicosen Unterschenkelgeschwüre, *Dermat. Wchnschr.* 79:1436, 1924. Dunballen, M. T. Traitement simple et efficace des ulcères variqueux de la jambe, *Bull. méd., Paris* 27:316 1910. Ledo, E. Resultats du traitement des ulcères variqueux par le plomb en lame in *Comptes rendus des seances publiés par le Dr. Svend Lomholt* Copenhagen, Engelsen & Schrøder, 1931, p. 835.

bandage up above the ankle in a figure of eight and repeat a few times as needed, until the whole foot and the lower part of the leg are covered with the bandage. It is advisable to cut off the bandage now and again in order to get a more even dressing, according to the configuration of the leg, without pulling the bandage unevenly. Apply the bandage so that one layer covers one half of the former layer and they both form a solid and uniform mass. Such a dressing can if necessary be worn for two or three months before removal. It is possible to treat the ulcer locally without removing the supporting dressing by cutting a window in the bandage. A water-tight rubber bath boot, now on the market, enables the patient to bathe and provides a water-proof protection for the zinc-gelatin bandage.

Only when the surrounding tissue of an ulcer is covered by eczematous lesions which ooze severely is local treatment, consisting of dress-



Varicose ulcers of the leg *A*, before treatment, *B*, three weeks after treatment

ings wet with boric acid or painting with methylosaniline (gentian violet) (2 per cent aqueous solution), needed.

It is understood that the varicose ulcer, owing to its varying causation, shows remarkable differences in its process of healing, depending on whether the ulcer was caused by chronic congestion or by thrombophlebitis or whether it is situated in pathologic tissue or in relatively normal skin. Often the small but deep crater-like ulcers usually found in highly inflamed, reddened and swollen skin which are caused by thrombophlebitis have shown a tendency to heal slowly. It was even found in some cases that such ulcers would not respond to several weeks of treatment and that sometimes during that period they would even enlarge somewhat in spite of injections into the varicose veins, until finally they suddenly started to heal. This was no doubt due to the fact that the inflammation at the root of the ulcer had been arrested. Flat ulcers surrounded by heavily damaged

eczematous and erythematous, or also by atrophic or callously hypertrophic, tissue showing little edema and often covered by thick, hard crusts heal very slowly, while large deep ulcers caused by embolic occlusion of a vein and usually surrounded by relatively healthy tissue granulate quickly along the edges. One can observe these ulcers closing gradually under treatment, with granulation proceeding from day to day and covering a large area within a short time. It is amazing to see how an ulcer almost the size of the palm which previously failed to respond to every other therapy heals completely within a few weeks after sclerosis of the veins, treatment with silver leaf and bandaging while the patient is up and about. The photographs illustrate such a healing process. Seldom is a patient obliged to stay in bed even for a few days. There are of course ulcers which this combined treatment will not heal, and they are those which have been active for decades and which circularly cover a large portion of the lower part of the leg.

Thrombophlebitis of the leg can be treated successfully by local application of 10 per cent ichthammol-zinc paste and zinc-gelatin bandages without confining the patient to bed. In cases of this condition particularly, such a dressing should be worn for a long time.

If varicose veins are hidden in edematous tissue, a zinc-gelatin bandage is employed to bring down the swelling, and when the varicose veins are visible again they can be treated in the usual manner.

SUMMARY

- 1 Varicose ulcers heal satisfactorily when treated with a combination of obliteration of the veins, local treatment and compressive dressings.

- 2 Silver leaf is an effective stimulant for the healing process.

- 3 Ready made zinc oxide-gelatin bandages facilitate the application of the Unna's boot.

45 East Eighty-Fifth Street

DISSEMINATED LUPUS ERYTHEMATOSUS TREATED BY SULFANILAMIDE

REPORT OF FOUR CASES

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The syndrome known as disseminated lupus erythematosus has received increasing recognition in the recent literature. The cause of the disease remains unknown, and relatively little has been written concerning the treatment. It is the purpose of this paper to report some experiences with the use of sulfanilamide in the treatment of disseminated lupus erythematosus.

There is no known effective therapy for the disease. Most cases reach a fatal termination in from several weeks or months to several years. Stokes¹ stated that he had never seen a patient with disseminated erythematosus lupus survive for more than five years. It is difficult to prognosticate for a given case, but in general one can say that the prognosis is poorest in the exanthematous types and best in the less fulminating disseminated discoid variety. Most cases within the latter group are not fatal. Belote's² recent classification of lupus erythematosus, while based on clinical rather than on pathologic or etiologic evidence, is worthy of emphasis. Here several varieties of the disseminated form, i. e., disseminated discoid, exanthematous (acute and subacute), the Libman-Sacks syndrome and the Senear-Usher syndrome, are recognized. The group of cases described by Osler³ as erythema exudativum multiforme with visceral lesions is also included. This classification embraces within the concept of disseminated lupus erythematosus clinical examples of widely varying virulence and type and serves to eliminate much confusion in the minds of internists and dermatologists alike. It is obvious that in the consideration of a given therapy for the disease, the recognition of these several types of varying clinical behavior is of primary importance.

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1 Stokes, J. H. The Diagnosis of Disseminated Erythematosus Lupus, *M. Clin. North America* **10** 290 (Sept.) 1926.

2 Belote, G. H. Lupus Erythematosus Disseminatus. Its Present Status, *Arch. Dermat. & Syph.* **39** 793 (May) 1939.

3 Osler, W. On the Visceral Complications of Erythema Exudativum Multiforme, *Am. J. M. Sc.* **110** 629, 1895.

In the current popularity of sulfanilamide therapy and because of the virulent clinical nature of disseminate lupus erythematosus and its supposed relation to streptococci, treatment of the disease with sulfanilamide was inevitable. Only a few reports have been published, although it is probable that at the time of writing the symptom complex has many times been treated with sulfanilamide. One of the cases described by Ingels⁴ was an instance of the disseminate type and Wollenberg⁵ (1 case), Anderson⁶ (1 case), Abramowitz⁷ (3 cases) and Sulzberger⁸ (2 cases) reported improvement or cure of disseminated lupus erythematosus by sulfanilamide. Bloom⁹ and Cornbleet,¹⁰ on the other hand, have had indifferent or poor results. In most of their cases, however, the lesions were of the fixed type. In the cases of Wollenberg and Anderson the condition was acute and virulent (exanthematous), whereas in those of Sulzberger it was classified as subacute disseminate discoid.¹¹

There is no agreement in regard to dosage of the drug for erythematosus lupus, but most investigators have given small amounts except when the condition was of the fulminating type. Since sulfanilamide has been regarded as a photosensitizing agent, it seems paradoxical that apparent beneficial therapeutic effect has occurred in persons sensitive to light. This observation has excited comment by several observers.¹² Sulzberger¹³ offered the explanation that since it was sometimes possible to stimulate or depress (photosensitivity) with the same agent, sulfanilamide and other photosensitizing drugs used in treating lupus

4 Ingels, A. E. Lupus Erythematosus Treated with Sulfanilamide, *Arch Dermat & Syph* **37**:879 (May) 1938.

5 Wollenberg, R. A. C. Lupus Erythematosus Disseminatus, *Arch Dermat & Syph* **38**:295 (Aug) 1938.

6 Anderson, H. F. Fulminating Acute Lupus Erythematosus Cured by Sulfanilamide, *Arch Dermat & Syph* **38**:621 (Oct) 1938.

7 Abramowitz, E. W., in discussion on Wise, F. Discoid Lupus Erythematosus Undergoing Dissemination, *Arch Dermat & Syph* **38**:661 (Oct) 1938.

8 Sulzberger, M. B. Lupus Erythematosus Treated with Sulfanilamide, *Arch Dermat & Syph* **39**:610 (March) 1939.

9 Bloom, D., in discussion on Wise, F. Discoid Lupus Erythematosus Undergoing Dissemination, *Arch Dermat & Syph* **38**:661 (Oct) 1938.

10 Cornbleet, T., in discussion on Ebert, M. H., and Omens, D. V. Lupus Erythematosus Disseminatus Subacutus, *Arch Dermat & Syph* **39**:372 (Feb) 1939.

11 Sulzberger, M. B. Personal communication to the author.

12 Taussig, L. R., in discussion on Ingels⁴; Peck, S. M., in discussion on Astrachan, G. D. Lupus Erythematosus in a Patient with Lichen Planus, *Arch Dermat & Syph* **37**:1082 (June) 1938.

13 Sulzberger, M. B., in discussion on Astrachan, G. D. Lupus Erythematosus in a Patient with Lichen Planus, *Arch Dermat & Syph* **37**:1082 (June) 1938.

erythematosus might, under certain conditions, desensitize a person to light. The question has also arisen as to the wisdom of the use of a drug which may depress the bone marrow in a disease characterized by leukopenia. No ill effects in this regard have been observed in the cases here reported and, to my knowledge, none have been reported. It seems safe to assume therefore that the leukopenia of lupus erythematosus does not contraindicate the use of sulfanilamide. On the other hand, progressive leukopenia during the course of sulfanilamide therapy makes it advisable to discontinue the drug.

This report and previous ones are subject to the common criticism that none of the cases has as yet been followed for a sufficiently long time. Furthermore, one must constantly bear in mind the natural course of erythematous lupus, particularly its tendency toward spontaneous remission and exacerbation. It is with the fullest realization of these facts that the following cases are presented.

REPORT OF CASES

CASE 1—Mrs O M, a white woman aged 36, was first seen in the Cincinnati General Hospital in July 1934. At this time she presented a clinical picture of discoid lupus erythematosus with discrete scaly lesions of seven years' duration on the nose, cheeks, ears and arms. The diagnosis was confirmed by histologic examination of tissue from a lesion on the right arm. The general condition was good. The routine physical examination and roentgenograms of the chest showed no abnormalities. The patient was given palliative therapy and was not seen until three years later.

Again there was a typical picture of discoid lupus erythematosus with lesions distributed as before. The patient was given sulfanilamide orally, 1 to 2 Gm daily, and warned against exposure to the sun. She returned one week later with a generalized maculopapular rash and a story of chills, fever and arthralgia following ingestion of the drug. Sulfanilamide was discontinued and the reaction entirely subsided within a few days. The original lupus erythematosus lesions all but disappeared. The patient was acutely ill when seen two weeks later, she complained of fever, arthralgia and generalized eruption. A widespread erythema was present, with accentuation about the follicular orifices. The skin of the nose, cheeks, ears and neck was red, edematous and tender. There were edema and tenderness of the tips of the fingers and toes. There were petechial hemorrhages in many areas, particularly at the tips of the fingers. There was no history of undue exposure to the sun. Hitherto futile efforts to hospitalize this patient were now successful.

The general physical examination was negative except for what was apparently a functional systolic cardiac murmur. The liver and spleen were not palpable. On admission the white blood cell count was 5,100, the red blood cell count 2,900,000 and the hemoglobin content 12 Gm. The differential count was 53 per cent polymorphonuclear leukocytes, 2 per cent eosinophils, 41 per cent lymphocytes and 4 per cent monocytes. The Kahn reaction of the blood was negative, and the urine was normal and contained no porphyrin. Cultures of the blood were sterile. Roentgenograms of the chest and of various joints showed no abnormalities. Renal function tests gave normal results.

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The patient's temperature was 99 F on admission and rose to 100 F daily during the first week. Small blood transfusions were administered every other day, and on the fifth day in the hospital administration of sulfanilamide, 3 Gm daily, was begun. The temperature was normal forty-eight hours later and remained so during the next two weeks. The cutaneous lesions cleared. At this time, the



Fig 1 (case 1) —Patient on admission to the hospital in August 1937

drug was discontinued, and within a few days the temperature rose and assumed a definite septic character with daily peaks of 102 to 104 F. There was a flare-up of the cutaneous lesions and symptoms and signs of pleurisy appeared. After a week, sulfanilamide was again administered, and within several days the temperature was normal. The eruption and pleurisy subsided. When on another occasion the drug was stopped there was a prompt rise in temperature. Again the administration of sulfanilamide was followed by a return of the temperature to

The patient was observed during two and one-half months of hospitalization. For the first six weeks she was treated at intervals with sulfanilamide, approximately 3 Gm daily, the hemoconcentration reaching 135 mg per hundred cubic centimeters. The drug was not given during the last month of hospitalization, when supportive therapy and blood transfusions alone were administered. The temperature remained normal during the latter period, and pleurisy and the generalized eruption completely disappeared. The white blood cell count varied between 5,000 and 6,000 without significant changes in the differential count. The anemia failed to respond to therapy with iron, liver or yeast, the red blood cells ranging from 2,500,000 to 3,500,000, with 9 to 12 Gm of hemoglobin. Except for the pleurisy, no frank evidence of visceral involvement was observed. When discharged from the hospital the patient felt well and had gained 8 pounds (3.5 Kg).



Fig 2 (case 1) —Patient after treatment with sulfanilamide

She enjoyed excellent health until recently, when she was confined to bed at home with "flu." This illness consisted of fever, malaise, pains in the joints and sore throat. There was no cutaneous eruption. The patient was not observed during this period but returned to the dispensary after recovery. At this time she did not appear ill, but there was a definite follicular erythema on the arms and hands. The patient stated that this eruption appeared on the preceding day after unusual exposure to the sun. The temperature was 99 F, the white blood cell count was 4,600 and the red blood cell count was 3,200,000. The patient refused hospitalization and was given small doses (2 Gm) of sulfanilamide daily. Within the week the eruption had cleared, and the drug was stopped. The patient has been symptom free since, although the discoid lesions have remained unchanged. At the time of writing she has been observed for approximately twenty-three months after recovery from acute dissemination.

CASE 2—W P, a white man aged 36, a press operator, was admitted to the dermatologic service of Cincinnati General Hospital on April 27, 1938. He complained of a generalized eruption, arthralgia, transient attacks of sore throat, muscular pains and swelling of the face. These symptoms had been present intermittently for approximately nine months. No history of fever, chills or photosensitivity could be elicited. There was a history of a penile chancre in 1928, and beginning in 1934 the patient received vigorous antisyphilitic treatment for two years. There was no personal or family history of tuberculosis.

The patient appeared chronically ill on admission. There were decided redness and edema of the face, ears and neck. Numerous telangiectases were present in these areas. There was some follicular dilatation but little scaling and no plugging. Areas of the skin of the face appeared moderately atrophic. Petechiae and splinter hemorrhages were present at the tips of the clubbed fingers and about the ankles. Pale, elevated, discrete, scaly lesions of various sizes and shapes were seen on the dorsa of the hands. The physical examination disclosed generalized lymphadenopathy, chronically diseased tonsils and an enlarged nontender spleen.

Examination of the blood revealed 3,400,000 red blood cells, 12.8 Gm of hemoglobin and 3,600 white blood cells (repeatedly), with 50 per cent polymorphonuclear leukocytes, 1 per cent eosinophils, 46 per cent lymphocytes and 3 per cent monocytes. The urine was normal and contained a trace of porphyrin. Roentgenograms of the chest, the result of chemical examination of the blood, and cardiograms were normal, and blood cultures were negative. The Kahn reaction of the blood was negative. Histologic examination of the lesions on the arm and face were interpreted by Dr. Leon Goldman:

"Hyperkeratosis, atrophy and thinning of the epidermis and scattered areas of perivascular lymphocytic infiltration are present. Marked edema and separation of the collagenous fibers are seen. The connective tissue fibers show thickening, shriveling and loss of elasticity. There are excessive collections of chromatophores. Connective tissue stains are desirable. This section is compatible with the diagnosis of subacute disseminated lupus erythematosus."

On the eighth hospital day, treatment with sulfanilamide was begun, the patient receiving from 7 to 12 Gm daily for a period of four weeks. Despite these relatively large doses, the hemoconcentration failed to rise above 8 mg per hundred cubic centimeters. The patient was also given frequent small blood transfusions. The temperature ranged from normal to 100 F, and the number of leukocytes from 3,000 to 5,000. The anemia failed to respond to iron, liver or yeast therapy. There was little change in the extent of the cutaneous eruption, but the petechial hemorrhages disappeared. Subjectively there was also improvement of the sore throat, arthralgia and muscle pains. The splenomegaly persisted.

The patient was discharged of his own volition after two months of hospitalization. He was seen in the dispensary several weeks later and his condition was good. Unfortunately, he left the city shortly thereafter and has not been seen since. The latest report as to his condition was that he was working and was apparently symptom free.

CASE 3—L S, a white girl aged 20, was admitted to the medical service of the Cincinnati General Hospital on May 5, 1938, complaining of pains in the joints and an eruption. Her illness began about two months prior to admission with the acute onset of migratory polyarthritis. The eruption began shortly thereafter and was described as being erythematous, macular and involving the face, neck, trunk and extremities.

The past history was noncontributory, there was no history of rheumatic fever, chorea or frequent sore throats. There was no personal or family history of tuberculosis.

The patient was acutely ill on admission, with the temperature 101 F, the pulse rate 100 and the respiratory rate 22. There were exquisite tenderness and pain in the guarded right shoulder. Generalized lymphadenopathy was noted. The cardiac rate was rapid, but there was no enlargement or arrhythmia. A soft systolic murmur was heard over the pulmonic area. The chest was clear, and the liver and spleen were not palpable. A generalized erythematous maculopapular eruption was present, most marked on the "butterfly" area of the face, the anterior and posterior part of the chest and the dorsal surface of the hands and arms. The tissue overlying the distal phalanges of the fingers was edematous, reddened and extremely tender. No petechiae of the skin or mucous membranes were noted.

On admission the urine was normal. The red blood cell count was 4,200,000, with 10.5 Gm of hemoglobin. The white blood cell count ranged from 4,000 to 6,200, with 48 per cent lymphocytes. The Kahn reaction of the blood was negative, and blood cultures were sterile. The electrocardiogram revealed evidence of myocardial disease, and the teleoroentgenogram showed evidence of mitral disease. The pulmonary fields were clear. Tests of renal function gave normal results.

The patient's course was febrile, the temperature ranged from 99 to 100 F during the first four weeks of hospitalization, and the eruption and arthralgia persisted. On the twenty-fourth hospital day, the temperature rose sharply to 104 F, and there were clinical and roentgenologic evidences of pleural and pericardial effusion. Following this, the course was rapidly downhill. The temperature remained in the neighborhood of 102 to 105 F, and albuminuria, hematuria, leukocytosis and severe anemia developed. Death occurred on the thirty-sixth hospital day.

The patient was given sulfanilamide, approximately 5 Gm per day, during the twelve days preceding her death, but there was no appreciable effect from this belated administration of the drug.

The essential observations at autopsy included acute pericarditis and pleuritis, generalized lymphadenitis, toxic splenitis and hepatitis, fatty infiltration of the liver and cerebral congestion and edema. The pathologic diagnosis of the renal lesions was "toxic nephrosis." The so-called "wire loop" appearance of the glomerular tufts could not be demonstrated. No special stains were made. The walls of the small arteries and arterioles of the lymph nodes, lungs and spleen showed degenerative lesions with associated thrombus formation and hyaline thickening of the intima.

CASE 4—M W, a Negress aged 28, was admitted to the medical service of the Cincinnati General Hospital on Aug 23, 1936. She complained of cough, fever, pains in the chest of several days' duration and swelling of the eyes of about two months' duration. A cutaneous eruption had been noted for about a month preceding hospitalization.

The essential physical observations at this time consisted of hydrothorax on the right side, bronchopneumonia and edema of the eyelids. In addition, a maculopapular eruption involving the "butterfly" area of the face and the dorsal surface of the hands and arms was present. There were also a few hemorrhagic lesions about the ankles. Histologic examination of a papule from the arm revealed a normal epidermis, edema and separation of the collagenous tissue of the cutis and perivascular lymphocytic infiltrate.

Examination of the sputum and of the fluid from the pleural cavity did not reveal the presence of acid-fast bacilli. The guinea pig test was also negative for tuberculosis. There were persistent albuminuria (2 to 3 plus) and occasional granular and cellular casts in the urine, but no red blood cells were present. The specific gravity varied from 1.008 to 1.016. The white blood cell count varied from 6,000 to 8,000 and the red blood cell count from 3,200,000 to 4,000,000. The differential count was normal. The Kahn reaction of the blood was 3 plus, and the Wassermann reaction of the spinal fluid was negative. Studies failed to disclose impairment of kidney function. Blood cultures were sterile. Roentgenograms of the chest confirmed the findings of hydrothorax and bronchopneumonia but showed no evidence of tuberculosis.

The course was febrile, the septic type of temperature rising daily to peaks of 102 to 103 F. Therapy consisted of rest in bed, supportive measures and several injections of bismuth subsalicylate. The eruption subsided within a period of four to five weeks, but the patient remained febrile for nearly two months. There was still albuminuria when the patient was discharged from the hospital. She was not again seen until April 1939 when she was admitted to the dermatologic ward.

The patient was gravely ill on this admission. The history of the interval was meager. In the summer of 1937 migratory polyarthritis developed, and she was confined to bed at home for nearly a year. After this she was again ambulatory and free of symptoms until the fall of 1938, when she became ill with "flu." There had been no recurrence of the cutaneous lesions.

On examination she was emaciated, dehydrated and desperately ill. No eruption was present. There was generalized lymphadenopathy. The eyes were edematous. There were clinical findings of pleural thickening, but the physical examination was otherwise normal.

Roentgenograms of the chest showed pleural thickening but no parenchymal disease. Tests of the sputum were repeatedly negative for acid-fast organisms. The specific gravity of the urine varied from 1.020 to 1.160, and there was persistent albuminuria (2 plus). No red blood cells or casts were demonstrated, and renal function tests gave negative results. The white blood cell count fluctuated from 10,000 to 17,000 during the period of observation, and the differential count was normal. The red blood cell count varied from 3,500,000 to 4,000,000, and the hemoglobin from 8 to 10 Gm. The platelet count was 150,000, and the bleeding and clotting times were normal. The Kahn reaction of the blood was 3 plus. Routine agglutination tests for typhoid, paratyphoid and brucellosis were negative. There was no disturbance of the chemical composition of the blood, and cultures of the blood were sterile. Complete laboratory and roentgenographic study of the gastrointestinal system gave negative results.

The temperature curve was septic in character with daily peaks of 102 to 104 F. The patient had repeated attacks of what were apparently "visceral crises." Therapy consisted of several transfusions of whole blood and other supportive measures. During the fifth week of hospitalization, sulfanilamide in doses of 4 to 6 Gm daily was given. There was no appreciable influence of the drug on the temperature or on the course of events, and the patient went rapidly downhill and died on the forty-fifth day in the hospital without the development of a clinically recognizable complication.

At necropsy the diagnoses were "subacute and chronic myocarditis with severe myocardial edema and myocardial degeneration, proliferative diffuse glomerulonephritis, acute splenitis, chronic adhesive pericarditis and pleuritis, acute passive congestion of the lungs and abdominal viscera, slight vascular nephrosclerosis,

and mild chronic generalized lymphadenitis" Microscopic sections of the kidneys (stained with hematoxylin and eosin) were interpreted by Drs Ralph Johansmann and Edward Vincent of the department of pathology

"The glomerular tufts are generally bloodless and show swelling and proliferation of the endothelial cells The capillary basement membrane is generally thickened and hyalinized Some of the glomeruli show slight infiltration with polymorphonuclear leukocytes Precipitated serum appears in the capsular spaces, and Bowman's capsule is occasionally thickened, hyalinized and adherent to the

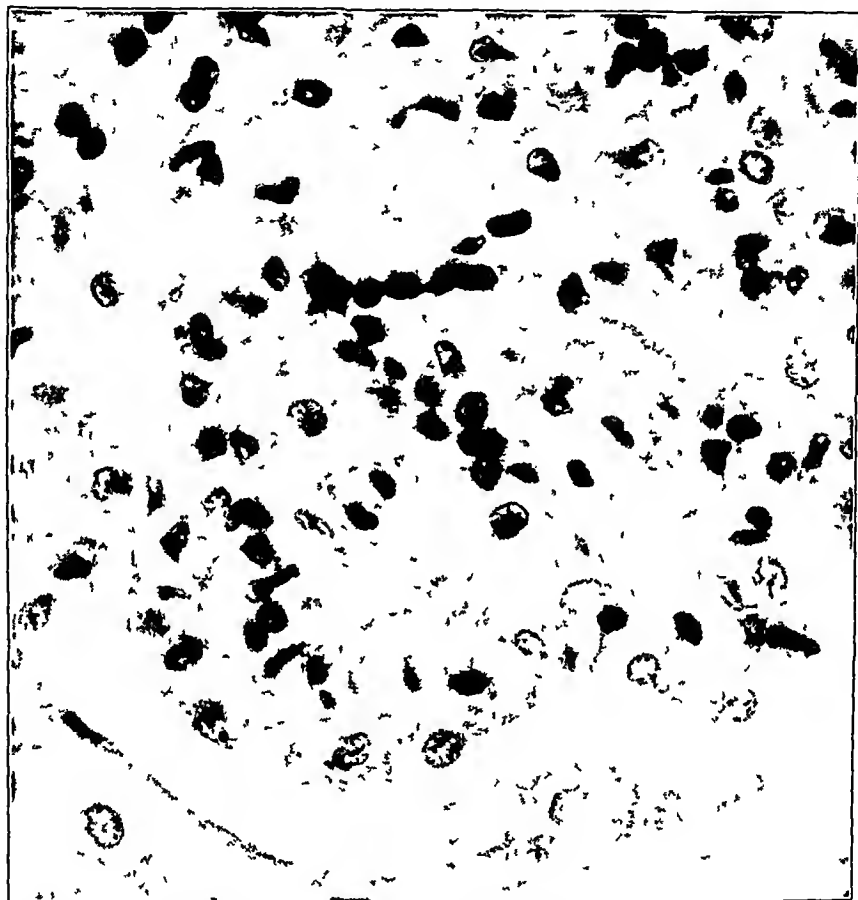


Fig 3 (case 4) —Photomicrograph (high power) of a section of the kidney stained with hematoxylin and eosin Note the avascularity and increased cellularity of the glomerular tuft and the hyaline thickening of capillary basement membranes

glomerular tufts Some glomeruli show almost complete hyalinization The tubules show advanced degenerative changes"

COMMENT

The conditions described herein were typical clinically of disseminated lupus erythematosus In each instance there was a characteristic eruption associated with visceral lesions, anemia and toxemia Three of

the 4 patients were young women, 1 was a Negro and 3 were white. In 3 instances leukopenia was a constant finding, and in the fourth relative leukopenia was present during the first period of hospitalization. In the 2 patients that died, the anemia had been resistant to iron, liver and yeast therapy and did not respond well to the transfusion of blood, and there was leukocytosis prior to death. At necropsy, pleuritis, pericarditis, splenitis and glomerulonephritis were the outstanding observations. Evidence of tuberculosis, active or healed, was absent. Renal changes similar to those reported by Baehr, Klempeier and Schiffrin¹⁴ ("wire loops") were demonstrated in case 4. These were not found in case 3, but it must be pointed out that no special stains were made. The diffuse arteritis in other organs, however, was of the same type described by the aforementioned authors.

In case 1 dissemination of the acute exanthematous type was superimposed on a long-standing discoid process. There was no apparent cause for this since there had been no infection, removal of foci or exposure to sun or ultraviolet radiation, and no gold had been administered. It is interesting to speculate as to whether the giving of sulfanilamide itself was not the precipitating factor, particularly so since, as in Ingels' case, dissemination of a chronic discoid process chronologically followed the administration of sulfanilamide, a photosensitizing agent. Again, when the initial immediate postsulfanilamide reaction had subsided there was great improvement in the original discoid lesions. That this patient was gravely ill and in great danger and that improvement or arrest of the disease occurred simultaneously with the administration of sulfanilamide could not be denied. The rise in temperature and the flare-up of the cutaneous lesions on two occasions when the drug was discontinued were suggestive as to its efficacy in this particular instance. This patient has now been followed for nearly two years and has enjoyed excellent health. If the relatively mild illness which she recently experienced can be looked on as a recurrence, the episode apparently was again controlled by sulfanilamide.

In case 2 therapeutic results were far less dramatic. This example is probably of the subacute telangiectatic or the disseminate discoid type of erythematous lupus, and as such the visceral and cutaneous manifestations were not so striking. The patient, nevertheless, showed improvement both subjectively in the amelioration of symptoms and objectively in the disappearance of petechial hemorrhages, following sulfanilamide therapy. It is regrettable that follow-up studies were so limited in this instance.

¹⁴ Baehr, G., Klempeier, P., and Schiffrin, A. A Diffuse Disease of the Peripheral Circulation Usually Associated with Lupus Erythematosus and Endocarditis, *Tr. A. Am. Physicians* 50:139, 1935.

In the last 2 cases sulfanilamide was not administered until the patients were dying, at which time the drug was entirely without influence. Case 4 seemed especially significant. From the early clinical record and from the necropsy observations, the diagnosis of disseminate lupus erythematosus was established. The death of this patient in the absence of cutaneous lesions was further evidence of a "lupus sine lupo" phase of the disease.

SUMMARY AND CONCLUSIONS

In 2 cases of disseminated lupus erythematosus in which sulfanilamide was administered the disease was arrested. One of the patients has been followed for nearly two years, the follow-up studies on the other were restricted to several months.

In 2 other cases of disseminated lupus erythematosus in which sulfanilamide was given in the terminal stages of the disease, no effect was noted. Necropsy in these instances revealed changes in the small blood vessels of the kidneys and other viscera of a type recently described as characteristic of disseminated lupus erythematosus and related clinical syndromes.

In the sulfanilamide therapy of lupus erythematosus, the drug should be administered early in the disease and in large doses, emphatic instructions to avoid sunlight should be given and all other precautions of sulfanilamide therapy exerted.

In view of this and recent similar reports and in view of the grave prognosis and unknown cause of disseminated lupus erythematosus, treatment with sulfanilamide or related compounds (sulfapyridine—i.e., 2-[paraaminobenzenesulfonamido]-pyridine) should be considered as a practical measure.

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CUTANEOUS METASTATIC CARCINOMA ORIGINATING FROM OSTEOMYELITIC CAVITIES

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The development of carcinoma in chronic osteomyelitic sinuses not only is uncommon but is very little appreciated by the dermatologist. The condition is well known to surgeons, however, and has been recognized for many years. Similar malignant degeneration may occur in tuberculous sinuses and also in chronic bronchial, biliary and anal fistulas, where an ingrowth of cutaneous epithelium to line the fistulas is not uncommon.

Credit for the first report of the development of carcinoma in osteomyelitic sinuses is somewhat difficult to assign. Dittrich¹ reported an authentic case in 1847, but it is probable that in 1 of the cases described by Hawkins² in 1835, under the title "Cases of Warty Tumors in Cicatrices," carcinoma had followed osteomyelitis. In the next forty to fifty years a number of reports appeared, and in 1891 Borchers³ collected reports of 20 cases from the literature and added reports of 5 cases of his own. In at least 14 of these 25 cases carcinoma had followed acute osteomyelitis.

In 1894 Devars⁴ collected a series of 39 cases and called attention to the fact that two clinical varieties of the disease may occur. He noted that the lesion appeared either as a superficial, easily recognized tumor or deep in the tissue, in which instance diagnosis was more difficult. During the following ten years many case reports appeared, but from

From the Section of Dermatology of the School of Medicine of the Division of Biological Sciences, University of Chicago

1 Dittrich. *Prag Vrtlschr* 2 161, 1847, cited by Benedict.⁷

2 Hawkins, C. Seven Cases of Warty Tumors in Cicatrices, *Med-Chir Tr* 19 19, 1835, cited by Benedict.⁷

3 Borchers, F. Ueber das Carcinom, welches sich in alten Fistelgangen der Haut entwickelt, *Inaug Dissert*, Gottingen, Dieterich, 1891, cited by Benedict.⁷

4 Devars, M. De la degenerescence cancroïdale des anciens foyers osteomyelitiques. Thesis, Lyon, no 933, Lyon, A. Rey, 1894, cited by Benedict.⁷

that time to the present the subject seems to have received little attention. A few instances of the disease were recorded, however, including those of Hitzrot ⁵ and Vernengo ⁶ in 1928.

In 1931 Benedict ⁷ extensively reviewed the literature and reported 12 cases in which carcinoma occurred in 2,400 patients with osteomyelitis treated at the Massachusetts General Hospital. Hellner ⁸ reported 3 cases in 1934. In 1936 Henderson and Swart ⁹ recorded 5 cases in which the patients were treated at the Mayo Clinic. These were the only patients in whom the condition was associated with malignant changes out of 2,396 patients with chronic osteomyelitis, a percentage somewhat less than that reported by Benedict ⁷. Additional cases were reported by Norinder ¹⁰ and Placinteanu and Dobrescu ¹¹.

Several facts concerning this condition are worthy of special emphasis. Development of carcinoma in association with chronic osteomyelitis is usually found in cases of long standing in which externally draining sinuses have been present for many years. Patients affected are predominantly in middle life or beyond, men are more frequently affected than women. The most common site of involvement is the lower extremities, especially the tibiae. It is stressed that metastases seldom occur and in any event rarely extend beyond the regional lymphatic vessels.

The exact pathogenesis of carcinomatous degeneration occurring deep in osteomyelitic cavities seems not to have been understood until recently. The theory most commonly accepted was that the continuous drainage of pus irritated the skin to such a degree as to cause malignant degeneration. This would satisfactorily account for the occurrence of carcinoma at the surface. However, this theory further assumed that in the deeply situated lesions the carcinoma had originated at the surface and grown downward. As early as 1847 Rokitsansky expressed the opinion that in Dittrich's case ¹ epithelial cells had grown in from the surface and had

5 Hitzrot, J. M. Epithelioma in Sinus of Old Osteomyelitis, *Ann. Surg.* **73** 247 (Feb.) 1921.

6 Vernengo, M. J. Epithelioma desarrollado en una fístula por osteomielitis crónica, *Bol. y trab. de la Soc. de cir. de Buenos Aires* **12** 801, 1928.

7 Benedict, E. B. Carcinoma in Osteomyelitis, *Surg., Gynec. & Obst.* **53** 1 (July) 1931.

8 Hellner, H. Fistelkarzinome auf dem Boden chronischer Osteomyelitis, *Fortschr. a. d. Geb. d. Röntgenstrahlen* **49** 109 (Feb.) 1934.

9 Henderson, M. S., and Swart, H. A. Chronic Osteomyelitis Associated with Malignancy, *J. Bone & Joint Surg.* **18** 56 (Jan.) 1936.

10 Norinder, E. Carcinomentwicklung bei chronischen osteomyelitischen, bzw. osteitischen Prozessen, *Acta orthop. Scandinav.* **8** 381, 1937.

11 Placinteanu, G., and Dobrescu, D. Fistelkarzinom auf dem Boden chronischer Osteomyelitis, *Zentralbl. f. Chir.* **64** 1447 (June) 1937.

caused the disease. It appears, however, that he too assumed that the cells were already malignant.

The recent independent investigations of Brunschwig¹² and Milgram¹³ have shown that chronic osteomyelitic cavities may become lined with stratified squamous epithelium owing to a downgrowth of the cutaneous epithelium along the draining sinuses. Although definite carcinomatous changes were not found in Brunschwig's cases, he considered the epithelial lining thus formed to be precancerous. He pointed out, further, that two factors operate to stimulate malignant degeneration of the epithelial cells, namely, their continued activity in attempting to line the cavities and the constant irritation to which they are exposed. The situation is thus not unlike that of carcinoma arising from chronic ulcers, in which attempted epithelial activity is likewise present in combination with constant secretion of irritating discharges.

The following case is reported as an instance of carcinomatous degeneration of the epithelial lining of a chronic osteomyelitic cavity, with cutaneous metastatic lesions of squamous cell carcinoma. It is unique in the fact that a careful survey of the literature failed to reveal previous reports of cutaneous metastatic lesions as the only clinical evidence of carcinomatous change in osteomyelitis.

REPORT OF A CASE

C W, a white man aged 37, was first seen in the dermatologic clinic Jan 12, 1939, at which time he complained of an eruption on the left arm and in the left axilla accompanied by severe pain on motion. The eruption had begun in July 1938 as two small nodules in the left axilla. Gradually numerous other nodules and papules appeared on the arm and forearm, arranged in a somewhat linear manner.

For the past twenty-five years the patient had suffered from chronic osteomyelitis of the left thumb. Four surgical operations on the thumb had been performed elsewhere, the last being in June 1938. At that time the remaining stump was amputated at the metacarpophalangeal joint. Unfortunately, no histologic examination was made.

When the patient presented himself in January for examination, two draining sinuses were present at the site of the amputation. Inspection of the left arm revealed nodular cutaneous lesions in the axilla and on the upper part of the arm, which extended along the flexor surface of the forearm to the wrist. The individual lesions were smooth firm reddish brown papules and nodules, varying in size from several millimeters to more than a centimeter in diameter. Their arrangement

12 Brunschwig, A. Epithelialization of Bone Cavities and Calcification of Fibrous Marrow in Chronic Pyogenic Osteomyelitis, *Surg, Gynec & Obst* 52:759 (March) 1931, Epithelialization of Chronic Osteomyelitic Cavities, *Radiology* 24: 627 (May) 1935.

13 Milgram, J. E. Epithelialization of Cancellous Bone in Osteomyelitis, *J Bone & Joint Surg* 13:319 (April) 1931.

showed a tendency to grouping. Some of the nodules in and near the axilla were tender on pressure, evidently owing to secondary infection, as evidenced by surrounding erythema and swelling. The eruption in its entirety bore a striking resemblance to herpes zoster (fig 1). General physical examination gave essentially negative results. The left epitrochlear and the left axillary lymph nodes were palpable. A roentgenogram of the chest showed no evidence of metastases.

Biopsy specimens obtained from two of the nodules, one on the forearm and the other in the axilla, showed identical microscopic pictures (fig 2). The epidermis was normal. In the upper half of the cutis and separated from the epidermis by a narrow band of normal tissue, was a rather well circumscribed mass of epithelial cells. Many of these cells were seen in the lymphatic vessels. The individual cells were large, with hyperchromatic nuclei and pale-staining



Fig 1—Upper part of the left arm and the left axilla, showing cutaneous metastatic lesions

cytoplasm. There was individual cell keratinization. Mitotic figures were found in moderate numbers. Cellular infiltration as a reaction to the epithelial cell invasion was practically absent. Blood vessels and collagen were normal. Diagnosis was made of metastatic carcinoma.

On Jan 31, 1939, an intrathoracohumeral amputation was performed by Dr Brunschwig, of the department of surgery. The patient made an uneventful recovery and was discharged from the hospital Feb 19, 1939. At the time of writing, he was still clinically well.

A microscopic section cut from the distal end of the first left metacarpal bone (fig 3) revealed a mass of malignant epithelial cells completely filling one small sinus and extending out to partially surround the bone. The cell nuclei were hyperchromatic, and a moderate number of mitotic figures were seen. Many of these cells were found within the lymphatic vessels. There was no pearl formation.



Fig 2—Low power photomicrograph of a nodule from the upper part of the left arm Hemalum-erythrosin-saffron stain



Fig 3—Low power photomicrograph of a section from the distal end of the first metacarpal bone of the left arm Hemalum-erythrosin-saffron stain

COMMENT

From what has been previously said, it would appear that the problem involved is of practical as well as of theoretic significance. There is sufficient accumulated evidence to allow one to assume that the epithelial lining of chronic osteomyelitic sinuses and cavities constitutes a precancerous lesion. The realization of the potential danger involved should be remembered when cases of long-standing osteomyelitis come under observation. Brunschwig,¹² in discussing the problem, stated

Most surgeons are now agreed that in elderly patients presenting extensive chronic osteomyelitis, amputation is justified when symptoms are severe. In such cases in which epithelialization of the bone cavities is present, amputation will also remove a potentially malignant lesion.

Since this form of carcinoma arises from stratified squamous epithelium, it should be of interest to the dermatologist. Moreover, as our case illustrates, the dermatologist may at times be the first called on to diagnose metastatic lesions and should therefore be familiar with the pathologic mechanism by which carcinoma develops in chronic osteomyelitic sinuses.

SUMMARY

Attention is called to the development of cutaneous metastatic squamous cell carcinoma arising from epithelialized chronic osteomyelitic cavities. The literature is reviewed and a case reported in which chronic osteomyelitis of the left thumb led, several weeks after amputation, to cutaneous metastases of squamous cell carcinoma. The same type of carcinoma was demonstrated in the lining of osteomyelitic sinuses of the metacarpal bone.

The significance of the newly formed epithelial lining of chronic osteomyelitic sinuses as a precancerous condition is stressed and the practical importance to the dermatologist emphasized, since the primary focus of the carcinoma may clinically not be evident.

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TREATMENT OF RAGWEED DERMATITIS

REPORT OF SEVEN CASES OF SUCCESSFUL TREATMENT WITH ABSOLUTE ALCOHOL EXTRACT OF RAGWEED LEAVES

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The first treatment of ragweed (contact) dermatitis was made in 1919 Hannah¹ reported good results in a single instance with coseasonal injections of an aqueous extract of ragweed pollen. In the same year, Sutton² reviewed 4 cases of the same condition, in 3 of which the patients were treated with a glycerin-phenol-saline solution extract of the pollen and showed decided improvement. However, none of these persons was given patch tests either with the oleoresin, which has since been proved to be the causative factor, or with ragweed leaves, which contain an abundance of the potent product. In 1930 Sulzberger and Wise³ noted improvement in 1 person following intradermal injections of water-soluble ragweed pollen antigen.

In 1931 Brown, Milford and Coca⁴ showed that ragweed (contact) dermatitis is due to the fat-soluble fraction of the plant or pollen rather than to the water-soluble fraction, which causes hay fever and pollen asthma. These observers suggested that treatment should be attempted with the oleoresin rather than with the water-soluble fraction. This they obtained by extraction of the plant with purified petroleum benzene (petroleum ether) and ethyl alcohol, dialyzing the extracted material, shaking it with carbon tetrachloride and adding tenth-normal sodium hydroxide to destroy the water-soluble antigen. This extract was dissolved in oil of almond and injected intramuscularly.

The reports of treatment with this extract have not been uniformly favorable. In the series of 24 patients treated prophylactically by

1 Hannah, L. Ragweed Dermatitis. A New Treatment with Preliminary Report of a Case, *J A M A* 72:853-854 (March 22) 1919

2 Sutton, R. L. Ragweed Dermatitis, *J A M A* 73 1433-1435 (Nov 8) 1919

3 Sulzberger, M. B., and Wise, F. Ragweed Dermatitis with Sensitization and Desensitization Phenomena, *J A M A* 94:93-95 (Jan 11) 1930

4 Brown, A., Milford, E. L., and Coca, A. F. Studies in Contact Dermatitis. I The Nature and Etiology of Pollen Dermatitis, *J Allergy* 2:301-309 (July) 1931

Brunsting and Williams,⁵ 19 had no relief of symptoms, 3 were doubtfully improved and only 2 had complete relief. Pascher and Sulzberger⁶ reported that 2 persons obtained relief, 1 remaining free of symptoms for several years, after preseasonal injections of the oily solution. Frank⁷ treated 1 person and was able only to reduce the itching for a few hours after each injection. Stroud⁸ obtained good results in several persons with thrasher dust dermatitis by injecting house dust oil and thrasher dust oil. Caulfield⁹ produced considerable relief in "tulip bulb" dermatitis by injecting an ether extract of the plant dissolved in Mazola (corn) oil. Rackemann¹⁰ stated that only three or four doses of the ether-soluble fraction of the plant oil are necessary for relief once the diagnosis is made. Rudolph and Deutsch¹¹ recently reported on a person suffering from dermatitis who gave positive reactions to patch tests with both timothy hay and ragweed pollen oils. Successful treatment was carried out by injections of a 20 per cent emulsion of the offending whole pollen grains in oil of almond.

In 1936, 2 subjects of the series to be reported on were treated with Lederle's oil-soluble ragweed allergen. Both showed considerable aggravation of symptoms and experienced no relief.

METHOD

For many years we have used with success Spain's extracts of *Rhus* leaves in absolute alcohol¹² in the treatment of dermatitis caused by poison ivy. Since the only difference between the rash caused by contact with the ragweed plant and that caused by the poisonous members of the *Rhus* family results from their different methods of pollination, we used a similar extract in the treatment of ragweed dermatitis. A quantity of ragweed plants was dried by air on the

5 Brunsting, L. A., and Williams, D. H. Ragweed (Contact) Dermatitis. Observation in Forty-Eight Cases and Report of Unsuccessful Attempts at Desensitization by Injection of Specific Oils, *J. A. M. A.* **106** 1533-1535 (May 2) 1936.

6 Pascher, F., and Sulzberger, M. B. Ragweed Dermatitis. Report of Two Cases, *Arch. Dermat. & Syph.* **28** 223-227 (Aug.) 1933.

7 Frank, J. J. Ragweed Dermatitis, *J. Iowa M. Soc.* **25** 283-285 (June) 1935.

8 Stroud, C. M. Allergic Dermatitis, *South M. J.* **28** 665-668 (July) 1935.

9 Caulfield, A. H. W. Tulip Fingers. Ragweed Dermatitis, *Canad. M. A. J.* **34** 506-510 (May) 1936.

10 Rackemann, F. M. Allergy. A Review of the Literature of 1935, *Arch. Int. Med.* **57** 184-212 (Jan.) 1936.

11 Rudolph, J. A., and Deutsch, M. Pollen Dermatitis. Report of a Case, *J. Allergy* **9** 187-188 (Jan.) 1938.

12 Spain, W. C., and Cooke, R. A. Studies in Specific Hypersensitiveness, XXVII. Dermatitis Venenata. Observations upon the Use of a Modified Extract from *Toxicodendron Radicans*, *J. Immunol.* **13** 93-112 (Feb.) 1927.

laboratory table and later on top of a dry air sterilizer. It was then broken up and immersed in absolute alcohol in the proportion of approximately 1 part of plant to 6 parts of alcohol and filtered through dry paper. Because of the nature of the solvent, sterilization seemed unnecessary.

At the time of injection, 0.2 cc of buffered saline solution was measured in a 1 cc tuberculin syringe. To this was added the desired quantity of alcoholic extract (not over 0.2 cc), and the syringe was filled with additional buffered saline solution. The active principle of the ragweed was immediately thrown out of solution in a finely divided suspension, giving the mixture an appearance of

Results of the Treatment with an Alcoholic Extract of the Ragweed Leaf of 7 Persons with Ragweed Dermatitis

| Name | H G | W G | J G | E J | J G | J J | M N |
|--|-----------------|------------------|------------------|--------------------|------------------|--------------------|------------------|
| Age | 52 | 44 | 31 | 16 | 60 | 32 | 50 |
| Sex | Male | Male | Male | Female | Male | Male | Male |
| Duration of dermatitis | 30 years | 7 years | 5 years | 12 years | 9 years | ? | 4 years |
| Season | July to October | July to November | July to November | August to December | July to November | August to November | July to December |
| Hay fever | 0 | 0 | 0 | 0 | ± | 0 | 0 |
| Asthma | + | + | 0 | 0 | + | 0 | 0 |
| Cutaneous reaction to aqueous extract of ragweed | + | + | + | 0 | + | ± | + |
| Cutaneous reaction to leaf or alcoholic extract | + | + | + | + | + | + | + |
| Per cent of eosinophils in the blood | 4 | 0 | 2 | 6 | 6 | 9 | 9 |
| Treatment | | | | | | | |
| Oil solution | | | | | | | |
| Prophylactic, 1936 | + | | + | | | | |
| Result, 1936 | 0 | | 0 | | | | |
| Alcoholic extract | | | | | | | |
| Prophylactic, 1937 | ± | | | | | | |
| Prophylactic, 1937 | | + | + | + | | | |
| Result,* 1937 | +3 | +3 | +3 | +2 | | | |
| Prophylactic, 1938 | 0 | | + | + | | | |
| Prophylactic, 1938 | 0 | + | | | + | + | ± |
| Result,* 1938 | +4 | +2 | +3 | +3 | +3 | +2 | +2 |

* Plus 4 indicates complete protection or relief. +2 and +3 varying degrees of partial relief.

greatly diluted milk. This suspension was immediately injected subcutaneously. The sting of the alcohol was only momentary and not very objectionable.

We believe that our success, in contrast to the failures of others, is due to the antigen entering the body in a suspension. In this way it is brought into immediate contact with a large number of body cells. When injected in oil it remains in solution and comes into contact with body cells much more slowly.

With city dwellers, whose only contact with ragweed is with the pollen carried in the air, the diagnosis is established by its seasonal appearance, coincident with the first appearance of ragweed pollen about August 1, and its great aggravation at the height of the season four

weeks later. In those accustomed to work or play in the country the rash will make its appearance on the extremities soon after the ragweed plants start to grow at the end of May. For such persons the diagnosis should be confirmed by a patch test.

In making a patch test a small piece of ragweed leaf may be used. We used this simple method in a number of persons, but the resulting dermatitis was much more severe than was necessary to establish the diagnosis. One drop



Patient (case 5) with ragweed dermatitis. The large area of dermatitis on the left shoulder was caused by a patch test with ragweed leaf. The smaller square on the right shoulder was produced by a dilution of the alcoholic extract of ragweed leaves.

of the 1/100 dilution of our alcoholic extract gave an adequate and much less annoying reaction. One hundred and twenty normal subjects (students) gave no reaction to the full strength extract.

The dose used in treatment was similar to that used for Rhus dermatitis.¹³ In phylactic treatment, we started with 0.025 cc of a 1/100 dilution. No untoward

¹³ Sharlit, H., and Newman, B. A. Specific Therapy in Rhus Dermatitis, *New York State J. Med.* **37** 61-63 (Jan. 1) 1937.

effects came from this dose, and a larger dose could probably have been tolerated. The relief from the itching was dramatic, although the rash usually remained until the end of the season. Prophylactic treatment was given to 3 persons, in whom the dermatitis was greatly diminished in extent and in intensity. One man went through a second season without additional treatment and with little discomfort.

An attempt has been made to separate contact dermatitis¹⁴ from the dermatitis or eczema occurring in persons and families suffering from asthma and hay fever. In our small group this difference did not exist. Two of the 7 patients were suffering from asthma at the time they consulted us, and another had had asthma in childhood. None had true hay fever, although 1 had mild and intermittent ocular symptoms during the season. Three had definite eosinophilia.

Four had definitely positive cutaneous reactions to aqueous ragweed extract in a dilution of 200 Cooke units per cubic centimeter, and 2 reacted to 2 500 units per cubic centimeter. The four stronger reactions were present on passive transfer. With the 1 possible exception just mentioned, none had hay fever. This is hard to explain. With the exception of the girl, all were outdoor laborers and had had much greater contact with both the leaves and the pollen than the average person. Again with the exception of the girl, the dermatitis developed in all of them much later in life than is the rule with hay fever.

It should be noted that the season does not correspond to the pollen season, although all 7 patients suffered most severely during late August and September. Prior to the appearance of pollen, the face was not involved. The persistence of the lesion into November and December is hard to explain. The ragweed plant maintains its vitality through most of October, and contact with the withering weed is possible until it is rotted by snow. The seeds, of course, are in the ground and maintain their vitality throughout the winter.

SUMMARY

Absolute alcohol extracts have been used with success in the diagnosis and treatment of ragweed dermatitis in 7 persons.

Prophylactic treatments were given to 3 persons. In all there was decided but not complete protection. In 1 person there was complete absence of symptoms the following year without any treatment, phylactic or prophylactic.

Seven phylactic or coseasonal treatments were given to 6 persons, and all 6 showed decided relief.

Four of 7 persons gave definitely positive intradermal reactions to aqueous extracts of ragweed pollen. In these persons reactions could

¹⁴ Engman, M. F., Jr., Moore, M., and Kile, R. L. Contact Dermatitis, *South M J* 28:442-444 (May) 1935.

be reproduced by passive transfer (Prausnitz-Kustner technic) One person had indefinite nasal symptoms during the hay fever season, and 2 had asthma throughout the year

The positive skin reaction to alcoholic extract of ragweed, as demonstrated by the patch test, could not be passively transferred to a normal person using the usual Prausnitz-Kustner technic

NOTE—Since this paper was written, we have the reports on 5 of the 7 persons during the 1939 season

E J received no treatment and had a mild rash on the neck and eyelids for only one week in September

W G had no prophylactic treatment A rash started July 25 Prophylactic treatment was begun August 10, with considerable relief

H G had only two injections in June He had no rash but said that his face burned for one week in September This was his second season of freedom

J G had three injections in June and one in September He had a mild rash on the forehead from August 20 to September 25

J J had seven injections from June 14 to July 19 and two in September A severe rash appeared in the middle of July, which disappeared There was a recurrence on August 23, and the rash lasted at least a month

LYMPHOGRANULOMA VENEREUM AFFECTING SIMULTANEOUSLY CERVICAL AND INGUINAL LYMPHATIC GLANDS

REPORT OF A CASE

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AND

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The virus of lymphogranuloma venereum is of decided lymphotropic nature¹ The inguinal lymphatic glands are most frequently affected in men and the perirectal lymphatic glands of Gerota in women² Occasionally both groups of lymphatic glands may be affected simultaneously in either sex Only rarely does one encounter reports of involvement of submaxillary, cervical or axillary lymphatic glands³ Axillary involvement occurring in surgeons has been reported, following an accidental inoculation of a finger received in operating on the buboes of lymphogranuloma venereum¹ Buschke and Curth in 1931⁴ and Curth in 1933⁵ reported involvement of the cervical lymphatic glands in 2 cases, in which the ordinarily transitory initial lesion of the genitals was replaced by an extensive, persistent ulceration of the mucous membranes of the tongue and the cheeks Both their patients said that they had indulged in acts of sexual perversion

Although generalized disease of the glands is said to be of fairly common occurrence in the early stages of lymphogranuloma venereum⁶ and although simultaneous regional glandular disease has been recorded,

From the Skin and Syphilis Service of Bellevue Hospital, service of Edward R Maloney, M D

1 Hellerstrom, S, and Wassen, E Hygiea 95 545, 1933

2 De Wolf, H F, and Van Cleve, J V Lymphogranuloma Inguinale, J A M A 99:1065 (Sept 24) 1932

3 (a) Bloom, D Lymphogranuloma of the Tongue and Cervical Lymph Glands, Arch Dermat & Syph 28 810 (Dec) 1933 (b) Rost, G Arch f Schiffs- u Tropen-Hyg 16 677 (Oct) 1912

4 Buschke, A, and Curth, W Klin Wchuschr 10:1709 (Sept 12) 1931

5 Curth, W Extra-Genital Infection with Virus of Lymphogranuloma Inguinale, Arch Dermat & Syph 28:376 (Sept) 1933

6 Pardo-Castello, V Lymphogranulomatosis Inguinalis, Arch Dermat & Syph 14:35 (July) 1926

I know of no previous record which states that both inguinal and cervical or submaxillary suppurative buboes were present simultaneously

Extragenital lymphogranuloma venereum of the submaxillary and cervical lymphatic glands usually occurs by infection through the mouth, being associated with sexual perversion. As a rule, when infection occurs in this manner the draining lymphatic glands follow the same chronic course and present the same clinical appearance as do the inguinal lymphatic glands. There is usually sore throat, and the common site of the primary lesion is the tonsil or the tongue.⁷

As is true of syphilis, entry by the extragenital portal, although rare, may occur more frequently than a study of the literature would indicate. It is probable that a greater number of extragenital infections will be reported in the future. The older name, lymphogranuloma inguinale, suggested the inguinal localization of the disease, to the exclusion of other regional lymphadenopathies.

In the case of our patient there was no history of sore throat or sore tongue, which in the 2 aforementioned cases preceded the cervical glandular involvement.

Our patient, who was first seen by us two months after his cervical lymphatic glands began to enlarge, differed from the patients reported on by other observers in that the oral cavity and the tongue did not disclose any lesion. The failure of detection of a primary lesion is not unusual, because this is a condition that frequently obtains when the infection is genital.⁸ The primary lesion on the genitals and the chronic vulvovaginal ulcerations are the most frequent sources of infection, although clinically free carriers have been important sources of transmission.⁹ In the majority of cases the initial lesion is herpetic, papular, nodular or ulcerative. It is usually small, inconspicuous and evanescent, appearing ten to twenty days after exposure. A urethritis may be the first manifestation of the disease.² Our inability to discover the initial lesion in our patient fits in with the usual clinical picture, whereas in both Buschke and Curth's case the primary lesion of lymphogranuloma venereum resembled in appearance and behavior the chronic ulceration of the labia, as seen in women.

The clinical appearance of lymphogranuloma venereum involving the cervical lymphatic glands alone is with difficulty differentiated clinically from tuberculous adenitis. This is especially true when no primary

7 Ravaut, P., Boulin and Rabeau. *Ann de dermat et syph* 5 463 (Aug-Sept) 1924

8 Sulzberger, M. B., and Wise, F. *Lymphopathia Venereum (Lymphogranulomatosis of Nicolas, Favre and Durand)*, *J A M A* 99 1407 (Oct 22) 1932

9 Frei, W. *Venereal Lymphogranuloma*, *J A M A* 110 1653 (May 14) 1938

lesion is found in the oral cavity in the former condition. The reaction to the Frei test in lymphogranuloma venereum and the finding of tubercle bacilli in tuberculous adenitis should determine the true nature of the disease in question.

REPORT OF CASE

W. B., a Negro man aged 62, born in the United States, a cook, was admitted to the service of dermatology and syphilology at Bellevue Hospital on Aug. 29,



Cervical buboes in a case of lymphogranuloma venereum in which the cervical and the inguinal lymphatic glands were affected simultaneously.

1938 and discharged on Sept. 30, 1938. His chief complaint was a painful swelling at the left angle of the jaw of two months' duration. Twenty years before admission he had had gonorrhea and was said to have had a syphilitic chancre, at which time he did not receive treatment for either condition. During 1937-1938 he had had several courses of treatment with neoarsphenamine and bismuth. His Wassermann reaction was positive.

He stated that about two months before admission he had had an outbreak of "boils." At that time a walnut-sized lump appeared on the left side of the face and neck at the angle of the lower jaw. Three weeks before his admission, about Aug. 7, 1938, it was aspirated by his family physician, pus was obtained and

the swelling decreased somewhat. Several days later the mass became painful and the patient applied a mustard plaster, causing the lump to become red and increasingly tender.

Physical Examination—On the left side of the face and neck at the angle of the jaw there was a somewhat painful walnut-sized violaceous swelling, indurated and with a soft teatlike elevation superimposed. Above and anterior to the ear in the parotid region was a smaller swelling of similar nature. Three fistulous openings discharging thin seropurulent material were present.

In the left inguinal region there was a shiny, smooth swelling the size of a hen's egg, slightly tender and indurated. As was true of the cervical swelling, the mass was attached to the overlying skin, which was bluish red. At points of suppuration there were three punched-out, draining fistulous openings. The scars of several healed sinus openings were present.

Laboratory Findings—Examination of material expressed through the sinus openings showed many macrophages and occasional lymphocytes and polymorphonuclear leukocytes, as well as fibrous shreds and granular debris. No tubercle bacilli were present, and no other organisms were found. Urinalysis gave negative results. The Ito-Reenstierna reaction was negative. A blood count showed leukocytes, 6,850, with polymorphonuclear leukocytes 65 per cent, transitional leukocytes 5 per cent, lymphocytes 31 per cent and eosinophils 1 per cent, and erythrocytes, 4,300,000.

The reaction to an intradermal Frei test (mouse brain antigen¹⁰), made on August 31, was positive. The reaction to an intravenous Frei test (mouse brain antigen) was positive.

An inverted Frei¹¹ test made with an antigen produced from pus aspirated from the patient's affected cervical lymph gland produced 9 positive intradermal reactions in 9 patients with proved lymphogranuloma venereum, all of whom also reacted positively to mouse brain antigen. There were 4 negative intradermal reactions to the Frei test both with the patient's antigen and with the mouse brain antigen in 4 patients who never had lymphogranuloma venereum. These patients were used as normal controls. Two of them had syphilis, 1 had pemphigus and the other had an inguinal adenitis of unknown cause. The antigen used for the intradermal tests was prepared according to the method of Frei. The aspirated pus was diluted ten times in a sterile solution of sodium chloride and heated in a water bath at 60 C for two hours on one day and for one hour on the following day.¹² The pus was tested for sterility. Since the inguinal buboes had ruptured before the patient was admitted to the hospital, no pus could be obtained for antigen.

On Sept 5, 1938, a week after the patient's admission to Bellevue Hospital, there developed in the left parotid region a tangerine-sized irregular swelling, nontender and nonfluctuant, from which a serosanguineous material was expressed. One cubic centimeter of a seropurulent discharge was aspirated on September 7. The reaction to the Mantoux test, with a dilution of 1:1,000,000, was negative.

Treatment—Treatment consisted of rest in bed and administration of five 5 grain (0.32 Gm) tablets of sulfanilamide three times a day for five days and three 5 grain tablets three times a day for seventeen days.

10 Grace, A. W., and Suskind, F. H. Lymphogranuloma Inguinale. Cultivation of Virus in Mice and Its Use in Preparation of Frei Antigen, J. A. M. A. 107:1359 (Oct 24) 1936.

11 Frei, W. J. Invest. Dermat. 1:367 (Oct) 1938.

12 Frei, W. Klin. Wchnschr. 4:2148 (Nov 5) 1925.

COMMENT

It is a matter of conjecture whether the enlargement of the cervical lymphatic glands was the result of an initial lesion of the oral mucous membrane following acts of sexual perversion or was due to involvement of this group of lymphatic glands as part of the generalized dissemination of the virus

We are of the opinion that the former explanation is more plausible, since our patient did not have generalized lymphadenopathy and because similar cases of extragenital lesion have been reported differing from ours only in that the primary lesion was extensive and persistent. This belief is further substantiated by the fact that the simultaneous occurrence of cervical and inguinal buboes has never been seen by us before in the service of dermatology and syphilology at Bellevue Hospital, in spite of the fact that a large number of patients with lymphogranuloma venereum are treated yearly.

Recently the number of patients under treatment for lymphogranuloma venereum in the service of dermatology and syphilology at Bellevue Hospital has quadrupled since routine Frei tests have been performed on all patients suffering from rectal involvement and from fistulas in ano. A positive Frei reaction is better evidence of lymphogranuloma venereum infection than absence of history of inguinal or cervical buboes.

SUMMARY AND CONCLUSIONS

A proved case of lymphogranuloma venereum is reported because of the rare simultaneous occurrence of cervical and inguinal buboes. Extragenital lymphogranuloma venereum must be considered in the differential diagnosis of all persistent regional enlargements of the lymphatic glands. The Frei test should be performed on all patients suffering from chronic inflammatory swellings of the lymph nodes, whether the swellings are situated in the inguinal, cervical or axillary region.

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OSTEOMATOSIS CUTIS

CARLISLE DIETRICH, MD

TACOMA, WASH

The purpose of this report is to present a dermatologic rarity. The patient was discovered incidentally during a visit to a syphilis clinic and already has been demonstrated at a meeting of the Philadelphia Dermatological Society¹

REPORT OF A CASE

J. H., a Negress aged 42, married and childless, exhibited a peculiar growth on the proximal phalanx of the fourth digit of the right hand. She had no other cutaneous blemishes or structural deformities.

The lesion, signet-ring-like, dorsally and laterally placed, was localized, nodular and slightly lighter than skin colored and measured roughly 1.5 by 1.5 cm. It consisted of fifteen to twenty closely aggregated nodules varying in size from that of a pinhead to about 4 mm in diameter. The larger ones projected prominently (4 to 5 mm) and the smaller ones less on the skin. Palpation disclosed additional nodules deeper in the skin and a stony hardness for the entire lesion. Tenderness, erythema and signs of inflammation were not discernible. The duration of the lesion had been lifelong and the patient said she sometimes picked small "stones" out of it. No member of her family that she knew of had any congenital malformation or anything similar to this.

Röntgenograms showed that the nodules were generally spheroid, opaque and "structureless." A bony spur also projected along the lateral side of the head of the fourth metacarpus and along the proximal third of the fourth proximal phalanx. The spur was not continuous with the bony substance of either bone but abutted against the head of the metacarpus similarly to a misplaced phalanx. It was about 1.5 cm long and half as broad, tapering toward the distal end and exhibiting the markings of spongy bone. The diagnosis was sesamoid or supernumerary digit (?).

The histologic examination was made by Dr. Weidman, who reported as follows:

"The epidermis is normal except for thickening of the stratum corneum. Immediately below the subpapillary layer and occupying the deeper parts of the corium is a well rounded nodule of bone 2 by 3 mm, bounded above by a distinct fibrous capsule. That this is periosteum is certain, as the osteogenic layer is definitely continuous with the bony matrix and its osteoblasts. Such a membrane cannot be clearly identified over the deeper aspects of the bone.

"The upper half of the bone consists of broad circumferential lamellas, which contain numerous and typical osteoblasts. In the deeper part seven or eight irregularly rounded spaces appear, around which more delicate circumferential

From the Laboratory of Dermatological Research, University of Pennsylvania

1 Dietrich, C. Nevus (Abortive Attempt at Polydactylism), Arch. Dermat. & Syph. 38:156 (July) 1938



Fig 1—The dark spot on the lesion is the healing wound left by removal of tissue for biopsy



Fig 2—Roentgenogram demonstrating the density of the bony particles and their relations to the finger and to one another



Fig 3—Low power photomicrograph showing the size and shape of one of the osseous nodules and its position in the depths of the corium



Fig 4—Photomicrograph illustrating the osteomatoid structure

lamellas can be identified. In this position the osteoblasts are far less numerous, more irregularly distributed and of a younger type. In short, the bone in the upper parts is definitely older.

"Some of the rounded spaces in the center of the bone contain but a capillary blood vessel or two, while the larger ones contain a few fat cells in addition. Red marrow elements are definitely absent.

"Microscopic examination shows that the spherical nodules observed clinically consist of compact bone. The circumferential lamellas at once suggest haversian systems. However, they are not regularly and systematically distributed through the bone, nor are the size and shape of the systems regular. Furthermore, the marrow cavity is sketchy to a degree. Ordinarily there would appear to be no alternative than to regard the small nodules as osteomas. They are highly atypical circumscribed osseous growths. However, it can be understood how a non-neoplastic process, too, could give rise to the same picture. Starting from the same point as in this case (the lesions were present in infancy), an irregular mode of growth, such as characterizes congenital malformations, could result in the picture here shown.

"In other words, this lesion is consistent with the concept of a nevus, viewed in the broadest light, particularly in view of the sesamoid (?) bone additionally revealed by roentgen rays. Of course, the bony masses may be parts of a supernumerary digit, but to prove this it would be necessary to demonstrate that they are part of a well organized structure, such as a digit, and they are not."

COMMENT

Primary Bone Formation—Primary bone formation in the skin has been occasionally reported. Becker² described an osseous plaque in the scalp of a woman aged 32, which was of fourteen years' duration and consisted of an infiltration of the connective tissue by bone rather than a distinct tumorous formation. Hypertrichosis, a keratotic nevus of the sole and a naevus pigmentosus of a finger were associated abnormalities of the skin. Becker cited the work of Sehit,³ who classified true ossification in the skin as (a) calcified simple dermoid cysts, (b) retention cysts which have become calcified, (c) true bone formed in the skin, (d) ossification of tumors (lipoma, lymphangioma or carcinoma), (e) formations with chronic inflammatory processes as the basis (syphilis and chronic dermatoses), and (f) stones of adipose tissue located in the subcutaneous tissue (sometimes cutis) of the extensor surface of the legs of old persons. Becker added the possibility of embryonal rests or atavism (suggested by the occurrence in a nevus), the association with extensive nevi elsewhere, the proximity of the tumors to the skull and their development during infancy.

² Becker, S. W. Osteosis Cutis, Arch. Dermat. & Syph. **10** 163 (Aug) 1924.

³ Sehit, E. Ueber Knochenbildungen in der Haut, Virchows Arch. f. path. Anat. **200**:395, 1910, cited by Becker.²

Plaques of bone in the scalp or on the aponeurosis of the skull, seemingly of primary genesis, have been mentioned by Hopkins^{4a} as reported also by Biuns, Strassberg,^{4b} Salzer^{4c} and Schaffer.

Heidingsfeld⁵ found numerous "miniature osteomas" lying between, but unconnected with, the hair follicles of a pigmented hairy nevus of the chin.

A bony plate of two and one-half years' duration, 1 cm thick and covering one third of the area of the sole of a 6 year old girl was discovered by Coleman.⁶

Multiple plaques and grains of ten months' duration were found by Taylor and MacKenna⁷ in the corium and subcutaneous tissue of the thigh, leg, chest, arm and scalp of a girl 15 months old, who had been a puny child not expected to live.

A chondro-osteomatoid infiltration in the skin below the ear of a 2 year old child was reported by Carl.⁸

Secondary Bone Formation—Whether in the skin or in any other tissue, secondary bone formation is dependent on degeneration of the tissue, calcification and a sufficiently vascular granulation tissue.

Multiple miliary osteomas of the skin of the face and neck, either following or coincident with a persistent acne or acneform eruption, were described by Hopkins,^{4a} who cited several others⁹ (Virchow, Wilkins, Cornil and Ranvier, and Sutton) as having observed similar or somewhat similar conditions.

Strassberg^{4b} described a bony plaque on the lateral aspect of the left leg of an old man who had hyperpigmentation and varicose veins. He

4 (a) Hopkins, J. G. Multiple Miliary Osteomas of the Skin. Case Report, Arch Dermat & Syph **18** 706 (Nov.) 1928 (b) Strassberg, M. Ueber heterotope Knochenbildungen in der Haut, Virchows Arch f path Anat **203** 131, 1911 (c) Salzer. Zur Casuistik der Geschwulste am Kopf, Osteoma cutis, Arch f klin Chir **33** 148, 1886

5 Heidingsfeld, M. L. Myomata cutis, Arch f Dermat u, Syph **92** 337, 1908

6 Coleman, W. Osteosis of the Skin of the Foot, J Cutan & Genito-Urin Dis **12** 185, 1894

7 Taylor, G., and MacKenna, R. W. Osteoma Cutis, J Cutan Dis **26** 449, 1908

8 Carl, W. Arch f Dermat u Syph **100** 183, 1910

9 Virchow, R. Die Krankhaften Geschwulste. Dreissig Vorlesungen gehalten wahrend der Wintersemester 1862-1863 an der Universitat zu Berlin, Berlin, A. Hirschwald, 1864, vol 2, p 103. Wilkins, M. Ueber die Verknocherung und Verkalkung der Haut, Gottingen, W. F. Kaestner, 1858, p 18. Cornil, A., and Ranvier, L. Manuel d'histologie pathologique, Paris, Germer-Bailliere & Cie, 1881 vol 1, p 270. Sutton, L., and Sutton, R. L., Jr. Diseases of the Skin, ed 9, St. Louis, C. V. Mosby Company, 1935, p 747, cited by Artz, L. Osteosis cutis multiplex, Arch f Dermat u Syph **151** 396, 1926. Weber, C. O., in Pitha, F., and Billroth, C. Handbuch der allgemeinen und speciellen Chirurgie, Stuttgart, Ferdinand Enke, 1882, vol 2, p 50.

suggested that prolonged hemorrhage from varices may eventuate in calcified hematomas which become ossified

Pollitzer¹⁰ observed bone formation in ulcerated sclerodermatous patches on the side of the face and neck of a man aged 47 and reasoned that in connective tissue fibers the succession of sclerodermatous changes proceeds through calcification to ossification

Trimble¹¹ reported osseous formation in an area on the buttock of a patient with lupus erythematosus

Whether the so-called primary instances of osteomatosis cutis are purely primary is open to question. The imagination need not be unduly stretched to envision a cutaneous nevus within which secondary bony metaplasia can occur on the same basis as elsewhere. On the other hand, it appears reasonable to suppose that genuine examples of primary ectopic bone can be observed within the skin as well as elsewhere, in view of the potential embryonal capacity of mesodermal tissue to form bone. This theory must be resorted to in cases in which it appears to be impossible to explain the bony formations in any other way.

SUMMARY

A congenital abnormality of bone formation is described, which resulted in a tumor-like swelling on the finger. Since it invaded the skin, the problem arises whether it should be designated as a nevus. However, as the formation had certain relations to a normal digit and was therefore an abortive normal structure and since it occupied other than a cutaneous position, the propriety of this classification is questionable. The name osteosis cutis is inadequate because it is such a broad term that it connotes diffuse bony as well as tumor-like formations. It seems permissible, then, from the purely clinical standpoint, to designate the lesion in my patient and any other projecting bony lesion of the skin the pathologic nature of which has not been determined as osteomatosis cutis. In short, the lesion in the case reported was osteomatosis cutis, which the roentgenograms demonstrated to be due to an abortive attempt at the formation of a supernumerary digit.

10 Pollitzer S. Ossification in a Case of Scleroderma, *J. Cutan. Dis.* **36** 271, 1918.

11 Trimble, W. B. Osseous Formation in Lupus Erythematosus, *Arch. Dermat. & Syph.* **1** 296 (March) 1920.

Clinical Notes

DERMATITIS DUE TO SAFETY PINS

Interesting Sequence of Sensitization Due to Contact with Nickel

JOHN GONWIN DOWNING, M D , BOSTON

Dermatitis due to contact with nickel has been reported in the past forty years by several authors¹, hence all dermatologists are conscious of it when searching for a cause of an eruption occurring in workers in industry. The history of wearing white gold spectacles, a wrist watch or nickel-plated garters often suggests a possible cause of the condition in other patients, but physicians are apt to forget



Reaction to a contact test with a safety pin, showing edema, erythema and vesiculation at the site where a pin had been held in place for sixteen hours

the innumerable other contacts which they have in their ordinary routine of life, such as those with nickel coins, key chains, electric light chains, cigaret lighters and paper clips. Doctors and dentists are constantly handling nickel-plated instruments. The young mother handling safety pins may forget such a contact, and the introduction of zippers on various articles of clothing presents a new contact in the daily lives of many. It is therefore deemed advisable to report the following case of sensitivity.

REPORT OF A CASE

Mrs P K noticed that after she had been caring for her first baby for about three weeks she was unable to close safety pins with the right thumb and index

¹ Lam, E S Nickel Dermatitis A New Source, J A M A 96 771-772 (March 7) 1931 Fox, H Nickel Dermatitis from Spectacle Frames and Wrist Watch, ibid 101 1066-1067 (Sept 30) 1933 Downing, J G Cutaneous Eruptions Among Industrial Workers, Arch Dermat & Syph 39 12-32 (Jan) 1939 Gilman, R L Nickel Dermatitis, J A M A 96 1331 (April 18) 1931

fingers, which had become so dry and cracked that this act was painful. She then used the third finger, which in turn also became disabled. As the baby outgrew diapers the condition disappeared, only to recur during the patient's care of her second and third babies. The summer before she consulted me, when she wore dresses which closed with zippers her skin became irritated at the sites of contact with these metals and it was necessary for her to remove them from her clothing. The following winter, while on a southern cruise she suffered intolerable itching at the sites of the fasteners of her garters, where she had a typical eruption due to contact with nickel. The condition responded readily to a treatment consisting of a change of the style of garter and of the use of soothing local applications. A contact test with safety pins showed a decided eczematous reaction.

COMMENT

Ninety-five per cent of safety pins are nickel plated, and the remainder, which constitute lingerie pins and baby pins, are of brass, dipped to give them a bright finish and coated with lacquer. The latter are supposed to be rustproof.

In the study of occupational dermatitides it has been noted that frequently nickel platers who have suffered from an eruption as a result of their trade become secondarily sensitive to leather and have a dermatitis on their foreheads and on the dorsa of their feet. This condition is resistant to treatment.

Perhaps some of the eruptions of the hands and feet which have been called fungous infections without cultural proof have started as a nickel dermatitis of the fingers with a secondary sensitization of the feet due to leather.

WINTER ECZEMA

C. C. CARPENTER, M.D., SUMMIT, N. J.

It was not until Niles published his paper "Winter Eczema of the Arms"¹ that I was able to classify a similar syndrome in several patients whom I had seen.

The purpose of my report is to draw attention to the fact that occasionally these same lesions may be found on the extensor surfaces of the lower extremities, as well as on the arms and shoulders, and I believe the title winter eczema more appropriate to describe this malady.

In all respects my experience with this disease of the skin has been similar to that of Dr. Niles. The small scaly circinate macules with a fine vesicular border are so suggestive of a superficial fungous infection that it is surprising that repeated microscopic and cultural studies have been without avail. There has been no history of exposure to contact irritants, other than excessive bathing, and only 1 patient has had a history of allergy. Seborrheic eczema has been considered as another possibility, but other evidences of it have been minimal,

¹ Niles, H. D. Winter Eczema of the Arms, *Arch. Dermat. & Syph.* 39: 474 (March) 1939.

and the patients have seemed to be made worse by therapy for this disease. Bath pruritus, as found in xerodermic skins, can be excluded, as the macules show no tendency to confluence and there are large areas of normal skin intervening. Data on the 5 patients whom I have observed are presented in the following tabulation:

| Patient | Sex | Age | Duration,
in
Number of
Winters | History | | Location | |
|---------|-----|-----|---|---------|-----------|----------------------|----------------------|
| | | | | Allergy | Xeroderma | Upper
Extremities | Lower
Extremities |
| 1 | M | 45 | 7 | No | Yes | + | + |
| 2 | F | 12 | 4 | Yes | Yes | — | + |
| 3 | M | 43 | 6 | No | Yes | + | — |
| 4 | M | 40 | 2 | No | No | + | + |
| 5 | M | 63 | 7 | No | No | + | + |

The basis of treatment is to reduce the number of soap baths and to exercise sufficient care in thoroughly drying the skin. Emollient ointments and liniments do not produce a lasting effect or adequately control the accompanying pruritus. At the suggestion of one of my patients, Dr J. K. de Vries, who has had this for two winters, I started the use of a proprietary remedy containing boric acid, oil of eucalyptus, sodium borate and essential oils in a hydrous wool fat and oxycholesterol-isocholesterol ointment base. The majority of the patients treated with this ointment have reported immediate improvement and by its continued use have kept recurrences to a minimum.

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ERYSIPELOID OF ROSENBACH SUCCESSFULLY TREATED WITH SULFANILAMIDE

ARTHUR G. SCHUCH, M.D., AND BEDFORD SHELMIKE, M.D., DALLAS, TEXAS

We wish to report briefly the cases of 4 patients with erysipeloid of Rosenbach treated with sulfanilamide. Three of the patients responded promptly to sulfanilamide alone and were well in from three to five days. The fourth patient did not respond to sulfanilamide by mouth but did respond to the immune serum injected locally at the advancing border of the lesion.

All patients were white men. Two received the infection from a puncture wound obtained from a fish fin, 1 from a beef bone and 1 from a hog bone.

The duration of the eruptions varied from eleven days to three and one-half weeks.

In 3 of the 4 patients the eruption involved approximately one third of the surface of the skin of one hand. In the fourth patient nearly all of the hand was involved.

The 3 patients that responded to sulfanilamide were instructed to take 10 grains (0.64 Gm.) of sulfanilamide four times a day. Healing required from three days

to six days for completion. Definite symptomatic improvement was noticed in all 3 patients at the end of the first forty-eight hours of sulfanilamide therapy.

The fourth patient, who failed to respond to sulfanilamide, continued taking the drug for one week. During this time there was extension of the cellulitis, and on the seventh day the immune serum was injected locally around the advancing border.

Routine Wassermann, Kahn and Kline tests performed on the blood serum of all patients were negative.

SUMMARY

Sulfanilamide alone in comparatively small doses produced prompt resolution in 3 of 4 cases of erysiploid of Rosenbach.

Obituaries

CHARLES NATHANIEL DAVIS, M D

1861-1939

Although Dr Davis was born in Philadelphia, on April 6, 1861, he spent all his early life, up to the age of 17, in the small Pennsylvania town of Pottsville. His schooling in Philadelphia started when he was 17, at Rugby Academy, followed by two years at the University of Pennsylvania. He then entered the medical school of the University of Pennsylvania, graduating in 1889, in the class that contained many men who became nationally and internationally famous. Shortly after his graduation in medicine he studied for six months in Vienna and spent a winter in attendance at the clinics in London.

For ten years he attended regularly the dermatologic clinic of Dr Louis A. Duhring and Dr M. B. Hartzell at the University of Pennsylvania as a voluntary assistant. In 1902 he organized a dermatologic service at the Pennsylvania Hospital. Although he had worked with Dr Henry W. Stelwagon at the Howard Hospital and had been consultant at the Germantown and at the St. Agnes Hospital, his great love in the field of dermatology was the old Pennsylvania Hospital, where he spent many hours each week.

He was a member of the College of Physicians and toward the end of his medical activities was elected to the American Dermatological Association, before which he presented the only scientific paper of his career on "The Use of Trichloroacetic Acid in Dermatology." Dr Davis was a wit; one of his favorite internal prescriptions was a laxative mixture which he had placed in the formula of the venerable Pennsylvania Hospital, a Quaker institution, under the designation "Quaker cocktail."

His name will always be associated with trichloroacetic acid for the treatment of keratoses, Labarraque's solution for various infections of the skin, salicylic acid and resorcinol in alcohol, which he designated "third rail," for peeling the skin, and a nongreasy base, containing stearic acid and a large portion of glycerin, devised in collaboration with Dr John Marshall, at that time Professor of Chemistry at the University of Pennsylvania.

Dr Davis had a great reputation for treating conditions of the scalp. One of his favorite remarks was that he could "grow grass on greens or hair on heads." This remark probably had its origin in his two great but diverse interests: the growing of grass, as chairman of the greens committee of the Philadelphia Country Club and also of the Cape May Golf Club, and his numerous dermatologic cases of defluvium capillorum.

His death, on Oct. 20, 1939, has removed a colorful, unusual personality, and he will be greatly missed.

FRANK C. KNOWLES, M D

Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

INTERMITTENT VENOUS COMPRESSION IN THE TREATMENT OF PERIPHERAL VASCULAR DISORDERS A REPORT ON ONE HUNDRED AND THREE CASES DAVID W KRAMER, Am J M Sc 197 808 (June) 1939

In a group of 103 patients with various peripheral vascular disorders treated with intermittent venous compression, benefit was obtained in 68 per cent. The author regards this method as a valuable adjunct in the treatment of such conditions.

BOECK'S SARCOID E F COTTER, Arch Int Med 64 286 (Aug) 1939

Cotter reports an unusual case in which generalized chronic infectious granulomas involved especially the myocardium. The course was rapid, the disease terminating fatally within eleven weeks of the development of symptoms. Because of the character and distribution of the lesions and an inability to demonstrate an etiologic agent, the diagnosis of Boeck's sarcoid was made. The skin showed only a single nodule on the forearm. Cotter states that the similarity between the myocardial lesions in this case and those in 2 cases of uveoparotid fever is impressive.

THIOCYANATE DERMATITIS MERVIN E GREEN and JAMES S SNOW, Arch Int Med 64 579 (Sept) 1939

Green and Snow present a case of the severe urticarial type of dermatitis medicamentosa due to potassium thiocyanate, a drug used in the treatment of hypertension. After eight days of therapy with this drug an erythematous maculopapular pruritic eruption appeared on the back of a patient. It later extended, and large wheals developed and persisted for about a week and then were followed by exfoliation and pigmentation. A number of points indicated that the reaction was allergic.

The authors had previously observed 4 or 5 cases of a mild, nondescript erythematous dermatitis in patients receiving this drug.

THE CLINICAL EVALUATION OF OVARIAN RESPONSES TO GONADOTROPIC THERAPY E C HAMBLÉN, Endocrinology 24 848 (June) 1939

Because of the increasing use of gonadotropic extracts and the many conflicting reports of the results of therapy, Hamblén reviews the entire field, with particular reference to clinical methods of evaluation of the various gonadotropic substances. Such data indicate that there exists little definite proof that therapeutic efficiency has been established for the gonadotropic substances in most patients with supposedly endocrinopathic gynecologic conditions. Augmentation of normally occurring ovarian responses may be produced by injections of gonadotropic extracts.

Hamblén describes a method of testing the efficiency of the gonadotropic substances.

STUDIES ON THE SENSITIZATION OF ANIMALS WITH SIMPLE CHEMICAL COMPOUNDS K LANDSTEINER and M W CHASE, J Exper Med 69 767 (June) 1939

In their experiments Landsteiner and Chase observed that the eruption appeared five days after application of 1% to the skin of guinea pigs. Extirpation of the treated area was unsuccessful in preventing sensitization if the excision was performed more than eight to twelve hours after the application.

In studying the manner in which sensitivity spreads over the skin in contact dermatitis, the authors were chiefly interested in demonstrating whether an epidermal pathway is necessary. If the cut surrounding the treated island of skin was deep enough to reach the muscles of the trunk, a general sensitization of the skin was not observed. However, if the cut was more superficial and the underlying cutaneous muscles were spared, then sensitization developed. The significance of the results was discussed in relation to the anatomy and physiology of the lymph vessels.

THE MANNER OF GROWTH OF FROG CARCINOMA, STUDIED BY DIRECT MICROSCOPIC EXAMINATION OF LIVING INTRAOCULAR TRANSPLANTS. BALDWIN LUCKE and H. SCHLUMBERGER, *J. Exper. Med.* **70** 257 (Sept.) 1939

The authors have applied the technic of microscopic examination with a slit lamp for observation of tumors implanted in the anterior chamber of the eye. The method allows observation of details of form of the tumor as well as arrangement of constituent cells and manner and rate of growth. The changes can be recorded objectively by photograph.

Lucke and Schlumberger conclude that neoplastic growth is not as anarchic as is suggested by histologic sections of some tumors.

LINCH, St. Paul

THE RHEUMATIC SUBCUTANEOUS NODULE AND SIMULATING LESIONS. H. KEIL, *Medicine* **17** 261 (Sept.) 1938

Keil reviews the early descriptions of rheumatic nodules and discusses the differential diagnosis of such nodules.

The typical rheumatic nodule is subcutaneous and is covered by intact skin, it is attached not to the skin but to the deeper structures. The nodules are more common with severe rheumatic fever and are almost always indicative of cardiac involvement. They are also more common with the more severe degrees of cardiac involvement—aortic lesions and pericarditis. The gravity of the prognosis roughly parallels the number and magnitude of the lesions. Children exhibiting rheumatic subcutaneous nodules have rarely been recorded as having lived to maturity.

The similarities and differences between subcutaneous nodules and Aschoff bodies are discussed. The former are macroscopically visible and palpable, the latter are microscopic. Necrobiosis occurs more commonly in the former than in the latter. The subcutaneous lesion is exudative, the lesion in the heart is proliferative. Multinuclear cells occur more often in the Aschoff body. This heals by scar formation, the subcutaneous nodule, sometimes by calcification. Supravital stains indicate considerable similarity between rheumatic nodules and the nodules of rheumatoid arthritis, and the author concludes that histologically the rheumatic nodule is not a specific lesion, with the possible exception of infiltrations in the galea aponeurotica, and that its recognition should be based on clinical criteria.

LIMPER, Louisville, Ky. [*AM. J. DIS. CHILD.*]

OSTEITIS TUBERCULOSA MULTIPLE CYSTOIDES AND SARCOID LESIONS. A. E. CONNOLLY, *Brit. J. Radiol.* **11** 25 (Jan.) 1938

In osteitis tuberculosa the pseudocystic areas are due to granulomas which replace the bony tissue and which at times may expand and even perforate the bony shell. The formation of sequestrums is rare, periosteal reaction is absent, and joints are usually not involved. The small bones of the hands and feet are the most frequently involved. The osseous changes are often associated with tuberculous manifestations in the skin.

Boeck described "sarcoid" lesions as a generalized granulomatous disease appearing as disseminated small nodes, grouped large nodular forms or a diffuse

infiltration The lesions predominate in the lymphatic system, lymphatic glands, tonsils, bone marrow, spleen, lungs and liver and also in the skin, where the dermatoses are recognized as Boeck's sarcoids. The lesions may be associated with tuberculosis, leprosy or syphilis. The granulomatous tissue, originating in the medulla, slowly permeates the bone, thereby producing various roentgenologic changes, depending on the extent of the change. Cystlike areas are usually located in the heads of the bones and are clearly defined and round, oval or heart shaped. The cavities may be central or peripheral. When they are peripheral, there is a localized distention of the bone in which erosion of the thin shell may produce a large cavity continuous with the soft parts. There is another form, a "Grille type," which is an exaggerated form of the diffuse type already mentioned. The lungs may be the site of abundant infiltrations about the bronchi and blood vessels. Sarcoid appears to be an infectious granuloma, occupying a place between tuberculosis and leprosy. Three cases are reported. In case 1, a 2 year old girl had tuberculous dactylitis, involvement of the radius, ulna, humerus and lower jaw and calcification of the intrathoracic glands. In case 2, that of a girl 16 years of age, there was tuberculosis of the dorsal portion of the spine. In case 3, a woman aged 34 had nodules on the hands and forearms, cystic changes in the hands and feet, increased hilar shadows and nodular infiltrations in the central parts of the lungs, and sarcoid.

SQUIRE, Chicago [AM J DIS CHILD]

STOMATITIS OF VITAMIN-B₂ DEFICIENCY TREATED WITH NICOTINIC ACID PHILIP MANSON-BAHR and O. N. RANSTORF, *Lancet* 2:426 (Aug 20) 1938

The authors report beneficial results with nicotinic acid in a woman aged 62 who for five years had had morning diarrhea. Stomatitis and glossitis appeared promptly after the onset, followed in eighteen months by parasthesias in one leg. She was twice admitted to a hospital for gastric ulcer, subsequently a diagnosis of sprue was made. Eventually she was placed on a full diet with an alkaline mixture and was given 150 mg of nicotinic acid daily. In ten days she was discharged from the hospital. Intolerance to the drug was discovered after ten days of administration, and the dose was reduced to 50 mg daily. The toxic effects continued. These consisted of stinging pain at the angles of the jaw and radiating to the ears, faintness and flushing of the face. This was followed by an "urticarial rash" on the chest, arms and thigh, which disappeared without treatment.

KRINSKY, Boston [ARCH NEUROL & PSYCHIAT]

WHITE FORELOCK: A NEW MUTATION A. M. NUSSEY, *Lancet* 2:947 (Oct 22) 1938

Cockayne in 1933 divided persons with white forelocks into (1) piebald persons (having unpigmented patches of skin in addition to the white forelock) and (2) persons with white forelock only. In both groups the abnormality is present at birth and as a dominant character is handed down direct from generation to generation. Occasionally the white forelock appears as a mutation in a family in which no such abnormality was known before, but once established its transmission occurs in the usual dominant fashion. Pearson recorded such an instance, and now Nussey records such a case of white forelock in a 10 year old boy.

LANGMANN, New York [AM J DIS CHILD]

MILIARY CUTANEOUS TUBERCULOSIS ASSOCIATED WITH MILIARY PULMONARY TUBERCULOSIS OF CHRONIC EVOLUTION R. DEGOS, R. PERROT and O. DELZANT, *Bull Soc franç de dermat et syph* 46:317 (March) 1939

The authors observed an interesting eruption in a child aged 6 years. It was generalized and consisted of small papules showing a yellow infiltration under diascopic pressure. The dermatosis was associated with miliary pulmonary tuber-

culosis, which in turn was remarkable because of its torpid, prolonged, apyretic character. The pulmonary infection was regarded as a primary one beginning after measles (turning of the cutaneous reaction to tuberculin).

The authors stated that the lesions were similar to those described by Tileston and by Lemer and Spieler. The histologic sections showed tuberculoid structure. Tubercle bacilli were found in the gastric contents.

"693" (SULFAPYRIDINE) AS A LOCAL APPLICATION. P. CUILFRET, J. PEILFRAT and J. PEISSERL, *Bull. Soc. franç. de dermat. et syph.* **46**: 597 (April) 1939.

The authors used sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) powder in the local treatment of pyoderma and also of impetigo, sycosis and vegetating bromoderma and iododerma. The crusts were removed, and the lesions were cleansed with distilled water and dried twice daily, then the powder and dry dressings were used. The results in all cases were satisfactory, equal if not superior to those obtained by the usual methods of treating pyogenic dermatoses.

PRELIMINARY NOTE ON THE USE OF "693" (SULFAPYRIDINE) IN LOCAL APPLICATIONS. GIRARD, J. DELBOS and R. JAUBERT, *Bull. Soc. franç. de dermat. et syph.* **46**: 603 (April) 1939.

Girard, Delbos and Jaubert used 20 per cent of sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) in either a stearate cream or equal parts of hydrous wool fat and petrolatum. The former vehicle was preferred for lesions on the face. The results were encouraging in cases of impetigo and sycosis, and the authors state the belief that the preparations had definite value in streptococcal and staphylococcal cutaneous infections.

LAMON, Minneapolis

SUBCUTANEOUS ADIPONECROSIS AND LIPOGRANULOMATOSIS IN AN INFANT. G. FROLA, *Arch. ital. di pediat.* **5**: 212 (June) 1937.

This is a report of a classic example of lipogranulomatosis subsiding after a longer course than usual (thirteen months). Histologically the lesions appeared in the deep layers of the dermis and the subcutaneous tissues and were characterized by a granulomatous reaction. There were numerous histiocytes in various stages, giant cells and zones of hyaline degeneration. The bibliography is extensive.

DOOLY, New York [*Am. J. Dis. Child.*]

A CASE OF HYPERNEPHROMA WITH CUTANEOUS METASTASES. A. MARTINS DE CASTRO and WALTER BUNGELER, *Arch. de dermat. e syph. de São Paulo* **2**: 77 (Sept-Dec) 1938.

The authors report a case of primary hypernephroma in the left kidney with metastases to the skin of the chest and the breasts. The cutaneous lesions were of two types. Of one type were the discrete nodules on the surface of the right breast. The other lesions manifested themselves as a diffuse extensive and deep infiltration of the skin of the chest and both breasts. The skin was dark red, thick, tender and scleroderma-like. The patient was a woman aged 67.

EXTRAGENITAL LYMPHOGRANULOMA VENEREUM, ON THE TONGUE AND CERVICAL NODES. RAMOS and J. SILVA, *Arch. de dermat. e syph. de São Paulo* **2**: 87 (Sept-Dec) 1938.

The author reports a case of extragenital lymphogranuloma venereum. A man aged 21 had a primary lesion on the tongue. Cervical adenopathy was observed, and the Frei reaction was positive. Histologic examination of the gland and the lesion on the tongue was made by Professor Favre, who made a diagnosis of lymphogranuloma venereum.

CIPOLLARO, New York

DERMATOGENOUS CATARACT A WINKLER, Arch f Ophth **139** 526 (Nov) 1938

To the many reported cases of cataract in young adults accompanied by cutaneous manifestations, such as eczema or neurodermatitis (Daniel, R K *Tr Sect Ophth A M A*, 1935, p 50), the author adds a case of his own A man aged 27 had been suffering from pruriginous eczema intermittently since the age of 4 Since reaching the age of 18 he had never been free from eczema Both lenses were cataractous (vision in the right eye, perception of light, vision in the left eye, 6/18) and showed, in addition to nuclear and cortical opacities, the subcapsular, anteriopolar, shield-shaped opacities characteristic of cataract associated with eczema Examination by the internist revealed abnormally high values for indican, tryptophan and phenolic substances in the urine A disorder of the gastrointestinal tract could be ruled out The urinary observations were interpreted as signs of abnormal protein metabolism The hepatic function was not impaired The possibility of the eczema being a manifestation of allergy was apparently not considered

KRONFELD, Peiping, China [ARCH OPHTH]

ERYTHRODERMA PROGRESSIVUM SYMMETRICUM (GOTTRON) OF CONGENITAL ORIGIN
H HULLSTRUNG, Dermat Wehnschr **107** 889 (July 23) 1938

A patient, aged 20, was observed in whom a cutaneous eruption had first appeared two months previously The eruption consisted of sharply margined keratotic erythematous areas on the extensor surfaces of the hands, feet, elbows and knees, on the posterior edge of each axilla, over the lumbar portion of the spine and around the anus While the condition suggested Brocq's *erythrodermie ichthyosiforme congenitale*, the hyperkeratoses of the palms and soles, the involvement of the face and the formation of bullae in the hyperkeratotic areas were absent Hullstrung believes the condition to be erythroderma progressivum symmetricum, as described by Gottron, and concludes that it is a congenital condition, though no similar disease was known to have occurred in other members of the patient's family

A CASE OF ACTINOMYCOSIS PEDIS A DÓSA, Dermat Wehnschr **107** 894 (July 23) 1938

Dosa describes a case of mycetoma in a 57 year old woman The organism was grown in aerobic cultures on malt agar and on blood serum agar and was classified as *Nocardia bovis*

MYCOSIS FUNGOIDES ATROPHICANS FOLLOWING A PREMYCOTIC STAGE WHICH
RESISTIBLES PRURITUS WITH LICHENIFICATION WILHELM MILBRADT, Dermat
Wehnschr **107** 923 (July 30) 1938

Milbradt reports tumors of mycosis fungoides on the generalized atrophic skin of a woman aged 46 At the age of 31 she had had severe pruritus with lichenification which was kept within the bounds of tolerance by treatment, though it had become generalized in recent years She gradually lost weight and died of intercurrent pneumonia

OCCIPITAL PUNCTURE IN THE HANDS OF THE DERMATOLOGIST BELA POLONY,
Dermat Wehnschr **107** 927 (July 30) 1938

The author believes that the majority of dermatologists are unnecessarily afraid of cisternal puncture He points out the advantages which permit of more frequent testing of the spinal fluid and states that with good technic and a proper regard for contraindications (severe arteriosclerosis, extensive tumor of the brain, deformity of the skull following injury and folliculitis of the nape) bad results need not be feared

KNUCKLE PADS WAITHER KRANTZ, *Dermat Wchnschr* 107 945 (Aug 6) 1938

The author describes knuckle pads, presenting photographs of the 2 he has observed. He reviews the literature on the condition, including Milian's report on *keratomes en nappe des mains* and Vorner's paper on *heloderma simplex et annularis* and states the belief that the diseases are the same.

CURE IN THE TREATMENT OF LUPUS C F FUNK, *Dermat Wchnschr* 107 973 (Aug 13) 1938

The author points out the difficulty of performing a satisfactory plastic operation to repair tissue destroyed by lupus vulgaris. He states the belief that in general the operations are unjustifiable, owing to the danger of lighting up the old process because of the lack of criterion of a complete cure. He prefers the use of a moulage-like prosthesis to repair large areas.

PATHOGENESIS OF HYPERKERATOSES IN GOLD DERMATITIS SIGMUND KOVACS, *Dermat Wchnschr* 107 977 (Aug 13) 1938

After seventeen injections of a gold preparation for pulmonary tuberculosis, a generalized erythematous eruption developed in a patient, with numerous hyperkeratotic wart-like lesions. Microscopically the lesions were indistinguishable from verrucae vulgares. The author considers three possible explanations for them: (1) the coincidental development of verrucae vulgares, (2) the possibility of a tuberculous origin and (3) the combination of the allergic response of the skin of the tuberculous patient with the biotropic effect of the gold preparation. He is inclined to accept the third explanation. TAUSSIG, San Francisco

NEW OBSERVATIONS ON IRITIS ROSACEA REPORT OF A CASE E OLAH, *Klin Monatsbl f Augenh* 100 714 (May) 1938

A man aged 54 had never suffered from any ocular condition until two weeks prior to his admission to the hospital. His left eye suddenly became reddened, and pain and photophobia of a minor degree were present, but vision remained satisfactory. The left eye showed slight injection, the cornea looked healthy and was free from precipitates. The peripheral zone of the iris was an even brownish gray, and the design was indistinct, the pupillary zone was of normal color, and the design was well defined. The pupillary reaction to light was sluggish. The pupil dilated promptly but moderately on instillation of scopolamine hydrobromide, only the pupillary zone being affected. The vitreous and fundus were normal. The dilatation of the pupil remained unchanged, although scopolamine hydrobromide was instilled daily. The peripheral, or ciliary, portion of the iris did not react until after the patient's recovery two months later. Obesity, facial rosacea and atrophy of one testicle were noted. Two brothers presented the same symptoms, whereas the patient's sisters were slender, and the skin of their faces was white.

Olah stresses the fact that rosacea was not observed in the conjunctiva or cornea, contrary to their involvement in the other 5 recorded cases of iritis rosacea. Hence, the iritis rosacea of Olah's patient was primary and was not the secondary result of a toxicity arising from the cornea, as pointed out by Salus. The endocrine origin was proved by the result of hormonal therapy, which consisted of injections of a combination of extracts of the thyroid and adrenal glands, the testis and the pituitary gland. A trial of this treatment is recommended in cases in which the condition is resistant to therapy, as it may be used without risk.

TREATMENT OF ROSACEA WITH EXTRACT OF THE CORTEX OF THE ADRENAL GLAND R THIEL, *Klin Monatsbl f Augenh* 102 394 (March) 1939

An ointment containing zinc ichthammol has yielded good results in keratitis caused by rosacea but has failed in many cases, some of which were reported by Claussen and by Wilhelm. Thiel refers to contributing disorders in rosacea, such

as subacidity, constipation, anemia and endocrine dysfunction, especially prior to or during the menopause, and mentions Wadel's satisfactory experience in cases of rosacea with extracts of the hypophysis and of the cortex of the adrenal gland. Two cases of Thiel's own observation are reported in which rosacea of the face with recurring keratoconjunctivitis resisted various treatments. Both patients, a man aged 43 and a woman aged 51, recovered promptly after injections of an aqueous solution of extract of the cortex of the adrenal gland prepared by a special method. The man received eight injections and the woman fifteen. Equally good results were obtained in 8 other patients. No untoward symptoms developed except in 1 patient, in whom small abscesses formed at the site of the injection, and they were attributed to local allergic reaction.

STOLL, Cincinnati [ARCH OPHTH]

A CASE OF NOMA WITH RECOVERY FOLLOWING ADMINISTRATION OF QUININE
ILCHENKO, Vrach delo 20 151, 1938

The noma occurred in an 8 year old girl in the course of influenzal pneumonia and was so extensive that the surgeons refused to undertake any operative procedure. In view of the grave prognosis given, the parents decided to take the child home. Ilchenko, however, was able to administer to her before her discharge two injections of a 10 per cent solution of quinine in doses of 3 cc each. A mouth wash of potassium permanganate solution was likewise recommended. Two weeks later the child came to the clinic completely recovered. The author, not having had the opportunity to try this form of therapy in a larger series of cases, urges other physicians to investigate along this line.

BODER, Los Angeles [AM J DIS CHILD]

Society Transactions

DERMATOLOGICAL CONFERENCE OF THE MISSISSIPPI VALLEY

EDWARD A. OLIVER, M.D., *in the Chair*

HERBERT RATTNER, M.D., *Acting Secretary*

Chicago, Sept 30, 1939

Psoriasis (Pustular) or Bacterid? Presented by DR FRANCIS E. SENEAR and
DR THÉODORE CORNBLEET, Chicago

Mrs C. L., aged 24, has had an eruption on the palms and soles for two years

At the present time the eruption is practically confined to the soles, particularly the left. The patches are sharply defined, superficial, reddish and scaly and are located at the tips of the toes, with a larger patch on the ball of the foot. Flat pustules are present as insets in the patches. The number of pustules varies from time to time. Three different examinations showed them to be sterile. There are no lesions elsewhere.

The eruption has been resistant to all forms of local therapy.

DISCUSSION

DR RICHARD WEISS, St. Louis. I think that Drs. Senear and Cornbleet were right in presenting this patient with a diagnosis of pustular psoriasis or bacterid. I was unable to make a diagnosis on one observation and have grave doubts that any one can readily make a diagnosis, even on more extended observation, in such cases.

DR HOWARD J. PARKHURST, Toledo, Ohio. This condition is stubborn, but I know of some instances in which the condition was cleared up after the removal of infected tonsils. Since this patient has never had a tonsillectomy, I think the tonsils might well be inspected.

DR HARRY R. FOERSTER, Milwaukee. I should like to express an objection to the practice of making a diagnosis of pustular psoriasis in cases of this type on clinical grounds alone. Unless there are typical lesions of psoriasis elsewhere than on the palms or soles, that diagnosis should be supported by histologic evidence of psoriasis.

DR JAMES H. MITCHELL, Chicago. The patient has typical pitting of the finger nails, such as occurs in psoriasis. I have a patient under observation who at first had classic psoriatic lesions on the trunk and lower extremities. These have cleared, and he now has lesions on the palm comparable to the lesions on the left foot in the case under discussion. I did not see any lesions comparable to those described by Andrews (Andrews, G. C. *Diseases of the Skin*, Philadelphia, W. B. Saunders Company, 1930, pp. 434-455), but I believe that the patient presented now has a psoriatic lesion on the sole and has had, and probably will have again, psoriasis in other areas.

DR THEODORE CORNBLEET, Chicago. I have inspected the patient's tonsils, and so far as I can tell they are not infected. This of course does not mean that their deeper tissues are not infected. The patient has not responded to any treatment directed against a fungous infection or against psoriasis.

Poikiloderma Atrophicans Vasculare, Dermatomycosis and Onychomycosis Presented by DR S W BECKER and DR M E OBERMAYER, Chicago

Mrs L S, aged 49, was first observed at the dermatologic clinic of the University of Chicago on Aug 4, 1939. She stated that she had had dry skin all her life and a pruritic vesicular eruption on the feet for the past four years. The eruption which caused her to seek medical advice had been present for about one year. It first appeared on the breasts as "brownish spots" and spread slowly but steadily to involve the entire breasts and the adjacent skin, the extremities and the lower part of the back. Subjective symptoms consist of slight pruritus and a feeling akin to pain.

The patient reported having been ill for years, with four "nervous breakdowns," which consisted chiefly of hysterical attacks of laughing and crying. She still cries at the slightest provocation, has pains all over her body, feels her heart beat fast, becomes nauseated and has lost about 18 pounds (8.2 Kg) in three months, despite an excellent appetite. She drinks considerable quantities of water and has nocturia (three to four times).

Physical examination showed moderate hypertension, tachycardia and a ventral hernia.

Examination of the skin shows plaques that are erythematous and telangiectatic, with scaling, definite atrophy and slight pigmentation. There are also a scaling eruption of the feet and thickening of the nails. Fungi were demonstrated in scrapings from the skin and large toe nails. The skin in several areas is ichthyotic.

Diagnoses of poikiloderma (Jacobi), epidermophytosis and onychomycosis were made.

The Kolmer and Kahn reactions were negative. Examination of the blood gave negative results except to reveal 7 per cent eosinophils. Urinalysis showed sugar (4 plus). Further investigation showed that the patient had definite diabetes mellitus, and she is now on diabetic management, without insulin.

Microscopic examination showed the epidermis to be thinned in its entirety, with practically complete loss of rete processes. The stratum corneum was thickened. The stratum granulosum was normal. The stratum mucosum was thinned irregularly. Directly beneath the epithelium, involving the superficial portions of the cutis, was a loose edematous infiltrate composed chiefly of round cells. In one area of its superficial portion near the epithelium there were some hyaline masses. The remainder of the cutis appeared normal.

DISCUSSION

DR PAUL A O'LEARY, Rochester, Minn. I believe that this patient has poikiloderma atrophicans vasculare. The cutaneous picture is not unlike that which Dr Becker recorded some years ago under the title of generalized telangiectases (Becker, S W. Generalized Telangiectasia. A Clinical Study, with Special Consideration of Etiology and Pathology, ARCH DERMAT & SYPH 14 387 [Oct] 1926).

Mycosis Fungoides Presented by DR J H MITCHELL and DR J R WEBSTER (by invitation), Chicago

J M, a white man aged 34, complains of an eruption of four and a half to five years' duration, with new lesions developing from time to time during that period, and as far as the patient has noted, none of the lesions have undergone involution. On interrogation the patient stated that he did not take drugs of any kind and then said he had taken an "Indian herb leaf tea" occasionally as a laxative but had not used any other cathartic. Until four months ago there was only occasional moderate pruritus, but since then some of the lesions on the legs have at times been pruritic, and there has been a burning sensation. The administration by mouth under our direction of a relatively large dose of phenolphthalein failed to modify the appearance of the lesions.

General physical examination gave essentially negative results. The lesions were and are now most numerous on the lower extremities, although the trunk

and arms are also involved to some extent. The patient has been under our observation since February 1939. During most of that period the lesions have been only slightly, if at all, elevated or indurated. However, in the last four months some of the lesions have become slightly thickened and palpably indurated. They are well defined, irregular patches of varying size and brownish red, the red component being clearer in some lesions than in others.

Histologic examination showed moderate hyperkeratosis and the presence of some leukocytes in the epidermis, but the important changes were in the corium. There was a cellular infiltrate, moderately diffuse, in the upper third of the cutis and fairly well defined at its lower border, although accompanying some blood vessels into the lower levels. The cells were predominantly lymphocytic, but there was much variation in size and in staining qualities, many of the cells having large clear oval nuclei. There were considerable pyknosis and some eosinophilic granular debris among the cells.

Examination of the blood showed 10,000 leukocytes per cubic millimeter, 50 per cent neutrophils, 2 per cent eosinophils, 2 per cent basophils, 45 per cent lymphocytes and 3 per cent monocytes.

The patient was presented before the Chicago Dermatological Society in March 1939 (*ARCH DERMAT & SYPH* 40 624 [Oct] 1939). After this he was given solution of potassium arsenite (Fowler's solution) up to 5 drops three times a day after meals for three weeks, but there was no change in the character of the eruption, then, because of gastrointestinal intolerance, this medication was stopped. Two exposures to roentgen rays, each of 75 r, with an interval of ten days between treatments, had no effect on the lesions on the back of the left leg and thigh. The only local treatment has been application of solution of calcium hydroxide. The only change during the period of our observation has been an increase in the degree of induration of some lesions during the last few months.

Mycosis Fungoides Presented by DR J H MITCHELL and DR J R WEBSTER
(by invitation), Chicago

E S., a white man aged 44, first noticed the gradual appearance of lesions on the trunk and extremities some time during December 1938. Pruritus was moderate at first, but as the lesions enlarged and became thicker, it increased in intensity until at times it was severe. He had been taking no medication by mouth, specifically no cathartics, nor had he received any injections. The only treatment used had been application of zinc oxide ointment locally. He was first seen by us on May 12, 1939.

At that time a general physical examination gave essentially negative results. The lesions were sharply defined, abruptly elevated, flat-topped papules and plaques, varying from the size of a pea to that of an adult palm. The average elevation was 1 to 2 mm above the level of the surrounding skin, and induration was perceptible. They were somewhat dusky red, and the surface carried a fine adherent scale. They were distributed on the trunk and the proximal portions of the extremities, with concentration in the regions of junction.

Histologic examination showed moderate acanthosis and some leukocytes in the epidermis. In the upper third of the corium, sharply limited below, was a diffuse, densely cellular infiltrate in a delicate stroma with dilated blood vessels. The infiltrate was distinctly polymorphous, with many cells with large, oval, clear-staining nuclei, but the cells were predominantly of the lymphocytic series. In certain areas there were considerable pyknosis and granular eosinophilic debris.

Examination of the blood showed 9,900 leukocytes per cubic millimeter, 63 per cent neutrophils, 2 per cent eosinophils, 1 per cent basophils, 33 per cent lymphocytes and 1 per cent monocytes.

From May 27 to June 19, 1939, the patient received in four treatments at weekly intervals a total of 220 r of unfiltered roentgen rays on the anterior portion of the trunk. Rapid and complete involution of the lesions occurred in this area, leaving some faint brownish stains at the sites of the lesions. Since then no

treatment other than local soothing preparations has been used. New lesions have appeared in areas previously clear, and those not treated have enlarged slightly. Within the last month some redness, thickening and scaling have appeared on the upper eyelids.

Mycosis Fungoides Presented by DR MICHAEL H EBERT, Chicago

L M, a Negress aged 39, presents a generalized pruritic eruption. She states that she first noticed an eczematous spot on the right biceps seven years ago, which appeared and disappeared, with severe pruritus. New eczematous patches appeared between the fingers and toes. These also were transient and recurrent. Weeping patches appeared about the nipples a little later. About a year and a half ago the lesions became more intense and more generalized. The present lesions have lasted for several months. Her personal history and family history are not significant.

General physical examination gave negative results. The spleen and the liver were not palpable.

The entire body, including the scalp, is beset with round or oval split pea-sized to finger-nail-sized, slightly elevated infiltrated plaques which are slightly scaly. Some of the lesions on the back are in the form of segments of circles, while other lesions in this region present keratotic follicular plugs. Several pea-sized to cherry-sized nodes are present in the axillary and inguinal regions.

Sternal puncture showed an increase in lymphocytic elements of 20 per cent. Examination of the blood showed 3,500,000 erythrocytes and 6,500 leukocytes per cubic millimeter, with 50 per cent polymorphonuclear neutrophils, 4 per cent eosinophils, 2 per cent basophils, 25 per cent leukocytes, 13 per cent monocytes and 6 per cent band forms. There was slight anisocytosis with hypochromia.

Histologic examination of a section taken from one of the lesions on the back showed a well defined band of cellular infiltrate occupying the upper half of the corium and separated from the acanthotic epidermis by a narrow band of normal tissue. The papillae closely approached the surface. The infiltrate was made up of a great variety of cells of various sizes, including lymphocytes and large and small reticulocytes, some containing large clear nuclei. Several mitoses were present and also a few eosinophils and basophils.

DISCUSSION

DR ELMORE B TAUBER, Cincinnati: A report was made that among the Negroes mycosis fungoides is rare. I have had 2 cases in which the Negroes were observed until their death.

DR RICHARD WEISS, St. Louis: Is it common for Negroes to have no pruritus in mycosis fungoides? This woman told me that she had never been bothered much with pruritus.

DR ELMORE B TAUBER, Cincinnati: My patients had severe pruritus.

DR CLARK W FINNERUD, Chicago: I think that every one will agree with the diagnosis in the last 2 cases in this group, clinically and histologically. The unusual case to me is the first one. When this case was presented before the Chicago Dermatological Society, as I remember, it created considerable discussion. From the section presented today I think that the condition cannot be diagnosed as mycosis fungoides. It seems to me to fit in well with parapsoriasis. An eruption of this character may subsequently develop into one of the types of lymphoblastoma.

DR HAMILTON MONTGOMERY, Rochester, Minn.: The first case in this group clinically presents the picture of a fixed drug eruption, but the histologic sections were typical for mycosis fungoides. The same is true of the case in which the condition clinically suggests parapsoriasis.

DR J R WEBSTER (by invitation), Chicago: I thought that there would be considerable discussion on the first case and probably differences of opinion but

that the general opinion of the condition on first examination would be a fixed drug eruption or parapsoriasis. We felt that we had ruled out the possibility of its being a fixed eruption by giving various drugs commonly associated with such conditions without modifying the eruption. In regard to parapsoriasis, we felt that in such a long-standing case there would be more epithelial changes than this picture shows and that the picture in the corium is definitely not that of parapsoriasis. All dermatologists are familiar with reports of conditions that for a long time presented the clinical picture of parapsoriasis and eventually became mycosis fungoides, and I feel that this is such a condition.

DR MICHAEL H. EBERT, Chicago The patient I presented complains of pruritus and also scratches a great deal. She states that the eruption started with weeping and lesions on the breast and later became generalized.

I have presented before the Chicago Dermatological Society, besides this patient, a Negro with mycosis fungoides (*ARCH DERMAT & SYPH* **33** 588 [March] 1936). The other eventually died of the disease. This is the first female patient. She presents keratotic follicular spines which did not show as much today as they have on other occasions. Similar spines were noticeable in one of the men I showed previously. Hematologic studies revealed no changes, but a sternal puncture showed a great increase in lymphocytes and lymphoblasts.

Lupus Erythematosus Presented by **DR ARTHUR W. STILLIANS** and **DR E. M. SMITH JR** (by invitation), Chicago

T. J., an Italian woman aged 33, has an eruption on the face, scalp and both shoulders. She stated that twenty years ago a papule appeared on the end of her nose and spread slowly over the nose. Five or six years later a red swelling appeared on the right cheek, which in the course of a few months became thickened and developed a crusted surface. There was a discharge from both these lesions. About the same time flat red lesions developed on the arms, these did not become thick or have a discharge but gradually formed soft scars. Twelve or thirteen years ago some thin flat pruritic areas developed in her scalp from which the hair soon fell and which slowly developed scar formation without discharge. The last lesions appeared two years ago under the jaw. The patient states that exposure to sunlight has always aggravated the lesions.

The scalp shows several areas of alopecia, with thin, rather sharply demarcated scars. On the nose and cheeks are well defined elevated tumor-like lesions, more numerous on the right cheek. They vary from dull purplish red to whitish areas of atrophic scar formation. The lesions are soft to firm and while involving the skin move freely over the deeper structures. There is no telangiectasia. The extensive scar on the lower part of the right cheek is soft. The bilaterally symmetric scars on the shoulders are thin, ovoid and soft, without a total loss of cutaneous markings.

A Mantoux test showed a strongly positive reaction. The Wassermann and Kahn reactions were negative. Roentgenographic study of the chest showed numerous deposits of calcium in the lymph nodes of both hilar areas, which may be in the glands or in the lungs and "no doubt represent an ancient tuberculous process." No active pulmonary tuberculosis was noted.

The condition of the patient has improved during the past two years by the use of alternating courses of gold sodium thiosulfate and 10 per cent bismuth sodium salicylate.

Microscopic examination showed little hyperkeratosis and no parakeratosis. The epidermis was thin and in places consisted of two or three layers of cells. The infiltrate consisted mostly of lymphocytes, with a few round cells and epithelioid cells. The infiltrate was somewhat scattered throughout the section but was more noticeable in the upper part of the corium and around half the hair follicles, blood vessels and glandular structures of the corium. The superficial blood vessels were widely dilated.

DISCUSSION

DR JOHN F MADDEN, St Paul I agree with the diagnosis I recently used sulfanilamide in the treatment of acute disseminated lupus erythematosus but had no favorable results

DR RICHARD WEISS, St Louis Was this patient presented with a diagnosis of discoid lupus erythematosus with dissemination? There were no examinations of the blood reported in the history I thought that the condition was a discoid lupus erythematosus and should like to know what the blood counts were

DR FREDERICK R SCHMIDT, Chicago The question came to my mind as to whether the condition was some form of sarcoid or angiolupoid, but today I thought the observations were consistent with the diagnosis offered

DR MICHAEL H EBERT, Chicago I did not see the section, but clinically the lesion on the face was like lupus pernio

DR MAURICE OPPENHEIM (by invitation), Chicago The lesions on the arm and face, I think, are not lupus erythematosus Some lesions are like atrophica maculosa Palpation of the lesions on the arm gives the impression of a hole, and the paper-like condition and the histologic observations are not those of lupus erythematosus The focus of round cells was lacking Stains of the elastic fibers would most likely prove that the condition is not lupus erythematosus, which is so often confounded with dermatitis atrophicans, particularly the superficial forms I should ask the presenters to regard this specifically in this case

DR CLARK W FINNERUD, Chicago I had the feeling Dr Ebert expressed about the lesion on the face I had not seen the condition on the scalp before, but I think it is a good demonstration of lupus erythematosus The histologic section was classic for that disease

DR E M SMITH JR (by invitation), Chicago We have tried to make a more accurate diagnosis of lupus erythematosus but have not succeeded The condition is difficult to classify Roentgenograms of the hands do not show any changes in the bones

Juvenile Xanthomatosis (Possible Hand-Schuller-Christian Disease) Presented by DR ERWIN P ZEISLER, Chicago

The onset of the disease in M F, a girl aged 9 years, occurred twelve months ago, with rapid spread and enlargement of the cutaneous lesions The eyes have recently become more prominent There is a history of thymus hyperplasia in the early part of her life and of some loss of weight recently There is a family history of diabetes

Neurologic examination gave negative results The liver and spleen are not enlarged There is moderate exophthalmos, the fundi and visual fields are normal

Examination of the skin shows numerous discrete flat and pedunculated chamois yellow tumors chiefly on the trunk, with fewer on the extremities, scalp and eyelids The results of dextrose tolerance tests are shown in the accompanying tabulation

| | First Test,
Milligrams per
Hundred Cubic
Centimeters | Second Test,
Milligrams per
Hundred Cubic
Centimeters |
|---|---|--|
| After fasting | 68 | 95 |
| ½ hour after administration of dextrose | 73 | 125 |
| 1 hour after administration of dextrose | 73 | 128 |
| 1½ hours after administration of dextrose | 74 | 111 |
| 2 hours after administration of dextrose | 75 | 99 |
| 3 hours after administration of dextrose | 74 | 96 |

The first test showed increased dextrose tolerance, indicative of pituitary disturbance The second test is probably correct

Examination of the blood showed 76.9 per cent hemoglobin, 5,160,000 erythrocytes and 12,850 leukocytes per cubic millimeter, with 53 per cent lymphocytes, 45 per cent neutrophils and 2 per cent eosinophils. Examination of the urine gave negative results. The Wassermann and Kahn tests gave negative reactions. Chemical examination of the blood showed

| | Milligrams per
Hundred Cubic
Centimeters | | Milligrams per
Hundred Cubic
Centimeters |
|--------------------------|--|-------------------|--|
| Dextrose (after fasting) | 85 | Free cholesterol | 88 |
| Nonprotein nitrogen | 30 | Cholesterol ester | 215 |
| Total fatty acids | 650 | Total cholesterol | 303 |

Röntgenographic examination of the skull showed exaggeration of the vein channels in the diploe of the frontal region and prominent digital impressions, probably of developmental origin. No defects were observed in the skull or in the long bones.

Histologic examination showed evidence of typical xanthoma.

There has been no result from a diet low in calories and fats except loss of weight. The tumors have continued to multiply and grow, although at a slower rate.

Juvenile Xanthoma Presented by DR OLIVER S. ORMSBY, Chicago

F. C., a girl 4 years of age, presents an eruption which began on one cheek when she was 3 weeks old. She has been presented previously before the Chicago Dermatological Society (*ARCH. DERMAT. & SYPH.* **36**: 207 [July] 1937, **38**: 267 [Aug.] 1938). When she was first presented there was a generalized eruption consisting of yellow and brownish yellow nodules and plaques of variable size on the scalp, face, lids, neck, trunk and extremities.

She is again shown to demonstrate the amount of involution the lesions have undergone. A large number, particularly on the extremities, have completely disappeared. Those of the face and scalp have flattened and largely cleared up. The largest ones on the trunk also show much diminution in size and loss of color. In many places pigment only remains.

DISCUSSION

DR CLINTON W. LANE, St. Louis: I thought that the condition in the case presented by Dr. Ormsby was juvenile xanthomatosis. Dr. Zeisler's patient may have Hand-Schüller-Christian disease, as the yellow xanthomatous lesions are accompanied by slight exophthalmos and possible beginning diabetes insipidus. The third member of the triad, a defect in the membranous bones, is not present. In a series of cases presented by an associate and me, none of the cutaneous lesions was yellow; in 1 case the eruption was hemorrhagic, in another, papular, and in a third, ulcerative. We believe that a more appropriate name for the members of the group of generalized idiopathic xanthomatoses is chronic (idiopathic) lipoidosis (Lane, C. W., and Smith, M., *Cutaneous Manifestations of Chronic [Idiopathic] Lipoidosis [Hand-Schüller-Christian Disease]*, Report of Four Cases, Including Autopsy Observations, *ARCH. DERMAT. & SYPH.* **39**: 617 [April] 1939).

DR HAMILTON MONTGOMERY, Rochester, Minn.: Dr. Zeisler's patient, I believe, shows definite early signs of Hand-Schüller-Christian disease. The typical triad of exophthalmos, rarefaction of the membranous bones and diabetes insipidus does not always develop early in the course of the disease. The child shows beginning signs of diabetes insipidus and exophthalmos. In Dr. Ormsby's patient with juvenile xanthomatosis it is interesting to note the involution that has occurred in many of the lesions. There is no evidence of systemic involvement, and the prognosis should be good. In patients with conditions like that in Dr. Zeisler's patient the prognosis is often serious. Not all patients with Hand-Schüller-Christian disease show elevation of the blood cholesterol level.

DR RICHARD WEISS, St Louis I should like to have Dr Montgomery's opinion about the cutaneous lesions in the patient he thinks has Hand-Schuller-Christian disease. The 2 patients whose conditions I have had the opportunity to study did not have the nodular lesions which this patient showed. The lesions were much more inflammatory, most of them were 2 to 5 mm in diameter and were somewhat necrotic in the center.

DR HAMILTON MONTGOMERY, Rochester, Minn Necrotic lesions like those that often occur in xanthoma diabeticorum have been referred to by Thannhauser as a secondary type of xanthomatosis associated with hyperlipemia, in contrast to the primary essential types of xanthomatosis. I believe that the lesions simply represent excoriations associated with pruritus. Dependent on the age, an individual lesion of xanthoma may vary greatly in size and in color, shading from light yellow to reddish brown. The size and shape of the individual lesion does not help in the diagnosis, but the distribution on the flexural or extensor surfaces and associated systemic manifestations of various types permit classification of the xanthoma. Classification is important from the standpoint of prognosis and treatment.

DR WILLIAM ALLEN PUSEY, Chicago Thirty-five or forty years ago I was interested in xanthoma. I had a patient with extensive xanthoma whose output of urine was enormous, but without sugar, and who had a definite disturbance of the pituitary body. I had simultaneously a typical case of diabetic xanthoma. So far as I know, up to that time no one had observed a case of xanthoma with diabetes insipidus. I thought I had familiarized myself thoroughly with xanthoma then, but now I feel like a stranger in a land where I do not understand the language. Hand-Schuller-Christian disease is utterly unknown to me in my present stage of ignorance, yet I do not think that much has been added to the general knowledge since then. My patient with xanthoma had a large lesion in the cornea and others in the larynx that almost killed him before he had a tracheotomy. I do not know whether there is so much difference in the knowledge of the disease as in the nomenclature, but I can testify as to the difference in the nomenclature.

DR ERWIN P ZEISLER, Chicago There are several interesting features in the case I presented. I first saw the patient about nine months ago, when the lesions were small and few and when there was decided obesity. Since then there has been a definite increase in the exophthalmos. Dr J H Hess, who has had the patient under observation recently, had the impression that the condition was Hand-Schuller-Christian disease. Recently Dr Lawless has had the patient under observation, and I should be glad to hear his opinion.

DR THEODORE K LAWLESS, Chicago I heard that Dr Becker had a preparation of pancreatic gland, lipocatic, so the patient was sent there for a trial of this material. She had been getting pancreatin in the meanwhile, and the mother stated the belief that the lesions were smaller.

DR OLIVER S ORMSBY, Chicago In the patient presented by me the lesions show great improvement. In this type of generalized juvenile xanthoma the lesions usually remain indefinitely. In a report on 122 cases of xanthoma tuberosum multiplex, McGraw (*Am J Cancer* 18:345 [June] 1933) observed 15 adults in whom the disease began in childhood. In the McDonough type (nevo-xantho-endothelioma) the lesions undergo involution comparatively soon and are usually few.

Leukoderma (Occupational) Presented by DR EDWARD A OLIVER, Chicago, DR LOUIS SCHWARTZ (by invitation), Washington, D C, and DR LEON H. WARREN (by invitation), Washington, D C.

H I, a Negro aged 44, is 1 of a group of 20 Negroes and Mexicans employed in a tannery, in all of whom the same type of leukoderma has developed within the last year. All have worn the same brand of rubber gloves. A similar condition was observed in other tanneries, plating works, factories manufacturing

electric apparatus and other places where this particular brand of gloves was worn. The ingredients used in the gloves and the method of their manufacture were obtained from the company making them. Patch tests performed on the affected workers with the different chemicals showed that an antioxidant caused positive reactions on all of them. A few days after the inflammation subsided there occurred definite depigmentation at the site of the reaction. The antioxidant is known by the trade name *agerite alba* and is said by the rubber company to be the monobenzyl ether of hydroquinone, containing less than 1 per cent of unchanged hydroquinone. In the patient's opinion four months were required for the depigmentation to develop.

Examination shows definite depigmentation of the skin of the forearms in the areas covered by the heavy rubber gloves. There is no depigmentation about the finger tips or on the palms.

Examination of the blood showed 4,740,000 erythrocytes and 7,900 leukocytes per cubic millimeter, 14.3 Gm of hemoglobin per hundred cubic centimeters and a color index of 0.9. The differential count was essentially normal.

The Wassermann test showed an anticomplementary reaction, the Kahn test gave a negative reaction. The pH of skin from the chest was 5 to 5.7.

DISCUSSION

DR S. W. BECKER, Chicago: This depigmentation is interesting, and I know of nothing in the literature that can compare with it. It is known that superficial burns will destroy melanoblasts and that in patients with the tropical disease known as *pinta* (or *carate*) permanent leukoderma develops. The depigmented plaques are first temporary and then become permanent. The chemical was in close approximation with the skin during periods of profuse sweating under the gloves, so it had a chance to enter the skin and produce the depigmentation. Whether the substance interfered with the action of the oxydase or could have interfered chemically with the mother stuff of melanin has not been demonstrated. The fact that the pigment is returning may mean that there are no organic changes.

DR MAURICE OFFENHEIM (by invitation), Chicago: I have observed many industrial diseases but never one like this. To me it was surprising to see such a condition in a Negro. The pigment is returning, which proves that the condition is not vitiligo, in which the pigment cells are no longer able to produce pigment. It is known that various superficial cosmetics are used to remove pigment, but no one is able to remove the pigment from nevi of various kinds. Only those pigmentations can be removed which are due to the pigmentation of basal cells but not if the melanoblasts are the reason of the hyperpigmentation. Dr Becker is right in supposing that there must be some fermentation or some other chemical process which is disturbing the chromatophores.

DR ARTHUR H. CONRAD, St. Louis: How long had the man been working in the tannery before this condition developed?

DR LEONARD F. WEBER, Chicago: Was there a preceding inflammatory change? What is the explanation of the lesions on the trunk if the chemical did not come in contact with that region?

DR EDWARD A. OLIVER, Chicago: I first saw this patient with 18 others in May 1939. All of them presented similar types of depigmentation on the forearms and in the areas covered by heavy rubber gloves, which extend up a considerable distance on the forearms. In some of them the depigmentation is more pronounced, and in others less so. One patient also presented patches on the buttocks, abdomen and chest, presumably due to contact with the gloves. Another presented several small areas on the right side of the face. In all the others only the forearms and hands were involved.

There was little if any inflammation preceding the development of the areas. In most of the cases patch tests with the antioxidant, *agerite alba*, gave positive results, that is, depigmentation occurred in the course of several weeks. There was apparently no loss of hair, but in 1 case there was pigment remaining about the hair follicles.

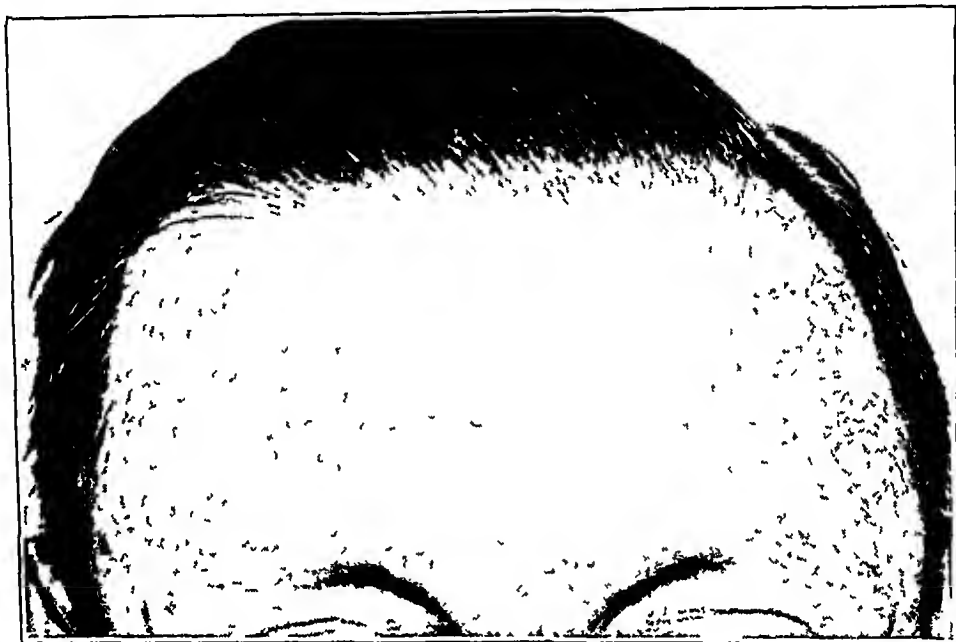
A Case for Diagnosis Presented by DR OLIVER S ORMSBY, Chicago

G E W, a man aged 44, presents white areas of various sizes on the forehead and the sides of the face and neck and behind the ears, which appeared three years ago. They become exaggerated when the patient stoops, when he is in a normal upright position they are much less distinct. No other changes are present, and during a year's observation no change has occurred. There is an incidental pruritus ani.

A photograph is exhibited which was taken by Dr James H Mitchell while the patient was suspended over a stepladder with his head hanging downward.

DISCUSSION

DR PAUL A O'LEARY, Rochester, Minn. I think this condition is unique. Three diagnostic possibilities came to mind when I looked at the patient. First, the lesions may be akin to a blush, a vasomotor instability in which the patient's



A case for diagnosis

position acts as the trigger. Secondly, I thought of the possibility of a mediastinitis, due either to a lymphoma or to syphilis, in which edema and congestion of the face occur when the patient stoops over. The third possibility, and a very remote one, is that of atrophic cirrhosis of the liver with associated pulsating spider nevi. I believe that the condition is a manifestation of a vasomotor neurosis, unusual in that a change of position is necessary to produce it.

DR S W BECKER, Chicago. When the patient stoops over there is a blush over certain areas, but in the upright position there are small, possibly telangiectatic, patches which remain. I produced friction, and the entire area which was rubbed became red, so the condition is not similar to a naevus anemicus. I think the pruritus ani is a part of the general functional disorder. I have had patients who flushed irregularly, and I think the condition in this patient could be explained on a vasomotor basis.

DR ELMORE B TAUBER, Cincinnati. My thought was that this condition is a vasomotor instability and that friction would produce the response.

DR CLARK W FINNFRUD, Chicago. This condition reminds me somewhat of the hypostatic process commonly seen in the legs. The definite change in color

when the patient bends over resembles in appearance such a hypostatic condition, in spite of the entirely different localization. The white areas may be dead white, and they are in this instance. Tuberculosis, syphilis and other infections can produce such vascular changes, of course, the process may be purely idiopathic.

DR FRANCIS E SENEAR, Chicago. I think that the first suggestion of Dr O'Leary's is the most likely answer. I believe that this condition fits in with the description of the morbid blushing which Dr Pusey called to my attention some years ago (Campbell, H. *Flushing and Morbid Blushing, Their Pathology and Treatment*, London, 1890, abstracted, Wood's M & S Monographs 7 253 [Aug.] 1890). I have been interested in such reactions ever since then, and there is considerable reference to them in the psychiatric literature, particularly in the French literature.

DR WILLIAM ALLEN PUSEY, Chicago. I do not understand how morbid blushing is any explanation for this condition. I do not believe that it makes one blush to lean over. There is, rather, a gravity situation to account for the congestion when a person is bending over. It occurred to me that the condition is a congenital anomaly, analogous to naevus anemicus. I conceive it as a disturbance of the blood supply of the skin, deficient in the pale spots and increased in the red. I think that the fact that Dr Becker rubbed it and the pale part got red does not preclude that explanation.

DR OLIVER S ORMSBY, Chicago. I have seen patients who had a peculiar vasomotor effect on the face in which transient flushing and blanching occurred. The condition under discussion differs entirely from that. In the patient the areas are permanently white and resemble those in naevus anemicus. When the patient's head is in the dependent position the white areas become more apparent, on account of the engorgement of the vessels in the surrounding skin. It seems that in the white areas the blood vessels are much reduced in number. That they are not entirely absent is proved by a reddening that follows the application of ice. The condition apparently has no constitutional background.

Arsenical Dermatitis (Chronic) Presented by DR EDWARD A OLIVER, Chicago

H N, a Negro aged 42, was admitted to the Veterans' Administration Facility on Aug 24, 1939. He was born in Tennessee and has had an eruption for the past nine years. His chief complaint is pain in the hands and feet and nodules over these areas. His occupation for years has been that of a molder. He admits that he has taken medicine frequently by mouth, the contents of which he does not know, but he states emphatically that he has never taken "drops." The general physical examination gave essentially negative results.

The skin of the entire body is dry and atrophic, and shows a reticular type of depigmentation. The fingers are covered with warty keratoses. The index finger of the left hand shows a large ulcerated squamous cell epithelioma. There is a similar lesion on the flexor aspect of the right thumb. There are also scaling keratotic lesions on the toes of both feet, with keratoses about the ankles. The skin on both heels is thin and tightly drawn.

Examination of the urine gave negative results. Examination of the blood showed 4,460,000 erythrocytes and 8,400 leukocytes per cubic millimeter and 80 per cent hemoglobin. The Wassermann and Kahn reactions were both negative.

DISCUSSION

DR NORMAN TOBIAS, St Louis. I think that this type of case is encountered all too frequently. Many of the patients in my experience give a history of having been treated for long periods for psoriasis, dermatitis herpetiformis or ichthyosis by physicians in rural districts. The younger generation of physicians is being taught more forcibly the danger of persistent arsenical medication. They also have more remedies at their command than the older ones. Another important

method of reducing the incidences of arsenical intoxications is to have the pharmacist place a "No Refill" label on every prescription containing an arsenical

DR FREDERICK R SCHMIDT, Chicago I think it is of interest that patients so often say that they have not taken arsenic by mouth and yet the cases are so frequent Several years ago I studied with Dr Oppenheim in Vienna, where I observed many cases, and frequently the patients told us that they had not taken arsenic when by examination of the hair the presence of the substance could be determined in excessive amounts

DR MAURICE OPPENHEIM (by invitation), Chicago I think that this question of arsenical dermatitis is a complicated one I have occupied myself during the last ten years working with these eruptions and have published three papers in collaboration with the chemist Dr Fantl (*Biochem Ztschr* 271 332, 1934, *Arch f Dermat u Syph* 170.488, 1934, 175 438, 1936) We found a high percentage of arsenic in the dyes of wall papers How the arsenic enters the organic system is an old question It is the opinion of some authors that entrance is made by way of respiration, others consider it via the intestinal tract, but examinations have shown that this is not correct I believe that arsenic enters the system in dust that is inspired The dye need not be green, it can be pink or yellow The arsenic is in pentavalent form in the wall dyes In the patients sometimes the hair or the nails or the scales contain the arsenic, in others it is in the epidermis and the connective tissue It is therefore necessary in every case to examine the hair, the nails and the scales, in addition to the urine and stools No doubt there is a type of melanosis in the case that is being presented, and I recommend examination for arsenic in the various structures I believe that the microchemical proof of the presence of arsenic in the tissue of the skin (Brunauer and Imemmesheimer and the American authors, Osborne, E D, *ARCH DERMAT & SYPH* 18. 37 [July] 1938, and Ayres, S Jr, and Anderson, N P, *J A M A* 110 886 [March 19] 1938) is not quite exact, according to my investigations

DR RICHARD S WEISS, St Louis Arsenic can be readily demonstrated in sections of the skin by means of spectroscopic examination

Sarcoid (Schaumann's Syndrome) Presented by DR OLIVER S ORMSBY, Chicago

L M, a white woman aged 31, was presented before the Chicago Dermatological Society at the annual meeting in January 1937 (*ARCH DERMAT & SYPH* 36 635 [Sept] 1937) At that time there were brownish red nodules and plaques on the face and forehead There were also lymphadenitis and a spinoventosa-like enlargement of the left ring finger Examination of the blood gave negative results, and there were no observations of clinical significance in the tonsils

At present brown discoloration remains in the affected areas on the face The adenitis has subsided, and the enlargement of the finger has decreased

Treatment has consisted of injections of gold sodium thiosulfate, arsphenamine and a salt-free diet The lesions have largely undergone involution, leaving brown pigmentation

Sarcoid (Schaumann's Syndrome) Presented by DR THEODORE CORNBLEET and DR HENRY C SCHORR (by invitation), Chicago

L H, a Negro aged 35, is presented with an enlargement of the lacrimal glands which developed five years ago Later enlargement of the parotid glands followed, together with obstruction of the nasal passages and symptoms referable to the larynx Still later swellings appeared over the phalanges of the fingers Lesions appeared on the skin two years ago

There are nodules varying in size from that of a split pea to that of a pea on the face in the region of the nostrils and on the arms The accessible lymph glands are enlarged, as are a few of the phalanges

Histologic examination of material from the lacrimal glands, the parotid and the nodules in the skin and epididymis showed changes compatible with a diagnosis of sarcoid

Roentgenograms of the hands showed the bones to be rarefied, and roentgenograms of the lungs showed diffuse infiltration of the hilar regions

Under treatment with intracutaneous injections of ascending doses of tuberculin there have been focal reactions, with accentuation of the cutaneous lesions, as well as of the other visibly affected areas, followed by gradual involution

Boeck's Sarcoid Presented by DR DAVID OMENS, Chicago

I H, a Negress aged 38, in February 1939 first noticed a flat papule on the face which was followed by multiple lesions of the same type on the forearm and above the right breast. The lesions have gradually increased in number over these areas. General physical examination gave essentially negative results.

The lesions vary from split pea sized to dime sized, with coalescence on the face. They are oval, flat and elevated from 1 to 2 mm, and most of them have a central depression.

Roentgenographic examination of the chest gave negative results. Examination of the sputum on three occasions gave negative results. There was a mildly positive reaction to 0.1 cc of a 1:10,000 dilution of tuberculin injected intradermally. The Wassermann and Kahn tests have repeatedly given negative reactions. Examination of the blood shows 5,290,000 erythrocytes and 5,850 leukocytes per cubic millimeter. A differential count showed 60 per cent neutrophils, 4 per cent eosinophils, 28 per cent lymphocytes and 8 per cent monocytes.

DISCUSSION OF CASES OF SARCOID

DR STEPHAN EPSTEIN, Marshfield, Wis. The white woman, I thought, presented typical lesions of sarcoid. I am not in a position to discuss sarcoid in the Negro, as this picture is different from the typical sarcoid that I have seen among white persons in Europe. The condition of the second patient, with ulcerations around the mouth, might fit into that clinical picture of multiple sarcoid-like granulomas in Negroes (Klauder, J. V. *ARCH. DERMAT. & SYPH.* 12:171 [Aug.] 1925), a disease which is apparently not rare in America and which has some relation to sarcoid and lupus miliaris.

DR FRANCIS W. LYNCH, St. Paul. This group of patients presents an interesting and instructive combination and variety of features. As in Dr. Ormsby's case, improvement is frequently recorded, but the value of therapy is still in question. In a talk at Minneapolis during his recent visit to this country, Snapper was enthusiastic as to the value of the administration of arsenic, placing considerably more emphasis on it than in his monograph (Snapper, I., and Pompen, A. W. M. *Pseudo-Tuberculosis in Man*, Haarlem, Netherlands, de Erven F. Bohn, 1938).

DR R. H. SCULL, Chicago (by invitation). The case of sarcoid in the Negress presented by Dr. Omens interested me, because it is a different manifestation of tuberculosis, often unrecognized in Negroes. I encountered a case for the first time at the meeting of this society in St. Louis in 1930 (*ARCH. DERMAT. & SYPH.* 23:1159 [June] 1931), at which time the condition was described as analogous to a type observed in some of the European races. Since then I have seen many patients with conditions of this variety, most of whom had been treated previously for secondary syphilis. The annular lesions occasionally observed on the scalp are often difficult to differentiate clinically from the annular lesions of syphilis. This type of sarcoid and its treatment have been described by Dr. Nomland (Nomland, R. *Hematogenous Cutaneous Tuberculosis [Sarcoid] in Negroes*. Report of Six Cases, *ARCH. DERMAT. & SYPH.* 30:59 [July] 1934).

I have under my care at present a Negress who has steadily improved with intracutaneous injections of old tuberculin. Her initial dose was 0.1 cc of a dilution of 1:1,000, her last treatment was with 0.4 cc of a 1 to 100 dilution.

Apparently there is a different type of immunology expressed in tuberculosis in the Negro.

DR S W BECKER, Chicago The woman presented by Dr Ormsby was under my care early in the course of the disease At that time she had an enlarged cervical lymph node and swelling of a bone of a finger, and she was advised to undergo treatment in a sanatorium Stokes recommends this type of treatment for cutaneous tuberculosis I question whether this patient can be much relieved while carrying on a strenuous occupation, as at present

DR OLIVER S ORMSBY, Chicago For a number of years it was difficult to understand what was meant by Schaumann's benign lymphogranulomatosis As a number of patients with this syndrome have been shown before this society, the condition is now clear Schaumann considered it a constitutional disease affecting the glands, skin and internal organs, particularly the lungs The cutaneous lesions are some type of sarcoid, either of the nodular or plaque type or lupus pernio The patient shown today was examined by Dr Becker, who performed a biopsy and demonstrated sarcoid histologically

A salt-free diet together with injections of tuberculin has accomplished much in this case The diet has also been beneficial in patients with erythema induratum and with other forms of cutaneous tuberculosis

DR THEODORE CORNBLEET, Chicago I am not prepared to discuss the fine points in the histologic structure differentiating these two diseases, but the gross evidence is characteristic of sarcoid I think the many clinical, laboratory and roentgenographic changes observed in the second case are overwhelmingly in favor of Schaumann's disease On the other hand, the man shows a definite focal reaction to tuberculin, and it has been taught that patients with sarcoidosis are not particularly sensitive to tuberculin I think that this case demonstrates the fact that tuberculin therapy may be of benefit in some cases

Recklinghausen's Disease Presented by DR DAVID V OMENS and DR WALTER W TOBIN, Chicago (by invitation)

B C, a white woman aged 47, stated that at the age of 25 she first noticed small lumps appearing over her body There were only a few at that time, but they have gradually increased in number until at present the skin is practically covered with them Some have remained small and skin colored, while others have enlarged greatly and vary from skin colored to bluish red On the patient's admission to the hospital, her sister stated that their parents and eight sisters had had no cutaneous eruption of any kind She also stated that the patient did not attend school beyond the sixth grade Her menstrual history is normal She has never married

General physical examination gave essentially negative results Her intelligence quotient is estimated as 25 per cent below normal

There is a universal distribution of skin-colored to bluish nodules of varying size, from that of a split pea to large pendulous masses which have a soft, doughy consistency Similar lesions are present in the mouth The hands and feet are unusually large, and the nails are thin and atrophic in some areas

Examination of the blood showed no abnormal results The Wassermann test gave a negative reaction The basal metabolic rate was +1 per cent Roentgenographic examination of the chest and of the bones gave negative results Examination of the urine showed negative results

DISCUSSION

DR NORMAN TOBIAS, St Louis I was surprised to note no cystic changes in the bones and café-au-lait macules The fibrotic plaque on the dorsum of the tongue should be watched for malignant degeneration My colleagues and I try to have patients with neurofibromatosis come in for an annual check-up, which includes a roentgenogram of the chest In 1 case a sarcoma of the rib was discovered

DR FRANCIS W LYNCH, St Paul I think that the facies and the observed enlargement of the hands and feet deserve some mention in that they suggest

acromegaly In Recklinghausen's disease exacerbations during pregnancy are common Such observations suggest that pituitary hyperactivity should be considered

DR DAVID OMENS, Chicago I called the attention of Dr Tobin to the fact that the patient has acromegaly of the hands and feet The first roentgen examination showed changes in some parts of the lung as well as in the heart

Leprosy (Cutaneous Type) Presented by DR MICHAEL H EBERT and DR A H SLEPYAN (by invitation), Chicago

Leprosy (Cutaneous) Presented by DR DAVID V OMENS and DR WALTER W TOBIN, Chicago (by invitation)

Necrobiosis Lipoidica Presented by DR THEODORE CORNBLEET, Chicago

S W, a white woman aged 56, states that during the past year an eruption developed on the lower part of both extremities The lesions began as red papules which coalesced with neighboring ones to form plaques The plaques have not been accompanied by subjective symptoms and have shown no tendency to clear

At present there are several plaques varying in size from that of a finger nail to that of a palm, reddish yellow in the center and brownish red at the periphery Telangiectasia is present throughout the older lesions The borders are infiltrated and firm, and the centers are shiny and depressed below the normal skin

Examination of the blood showed a normal blood sugar level Total blood lipids were 173 Gm, cholesterol esters, 211 mg, and cholesterol, 320 mg, per hundred cubic centimeters

Necrobiosis Lipoidica Diabeticorum Presented by DR THEODORE CORNBLEET, Chicago, and DR F W HETREED, Chicago (by invitation)

K S, a white woman aged 53, has an eruption of four years' duration The lesions first appeared as small glossy reddish macules, which increased in size by coalescence with neighboring lesions They are located on the legs and have yellowish centers, violaceous borders, telangiectasia and scaling

The Wassermann and Kahn tests showed negative reactions The blood sugar was 88 mg per hundred cubic centimeters The dextrose tolerance curve was normal The cholesterol content was 218 mg, and the cholesterol esters, 93 mg, per hundred cubic centimeters of blood The total lipids were 176 Gm A fat tolerance test with 50 Gm of fat at the end of six hours showed total lipids, 226 Gm

Histologic examination showed slight hyperkeratosis The papillary layer of the dermis was edematous, and in the reticular layer there were numerous tubercle-like structures composed of giant cells, endotheloid cells and lymphocytes, these structures were particularly noted about hair follicles and sweat glands The picture was suggestive of tuberculosis cutis

Sudan stain showed small accumulations of fat in the cornified layer of the epidermis and minute granules in some of the cells in the granulomatous lesions described These observations are in keeping with those in necrobiosis lipoidica

DISCUSSION

DR FRANCIS W LYNCH, St Paul Although there can be no question as to the correctness of the diagnosis in these 2 cases, the case that is more characteristic clinically has the less typical histologic picture, and the one that is less characteristic clinically has the more typical histologic picture In a case recently observed at the University Hospitals in Minneapolis the eruption in its early stages resembled localized neurodermatitis around the ankle, but the histo-

logic changes were typical of necrofibrosis lipoidica I think that it has been sufficiently emphasized that this condition is not always associated with diabetes

DR NORMAN TOBIAS, St Louis One of the patients had had arthritis for eight years Since certain types of arthritis are associated with elastic tissue degeneration of the joint capsule, there may be a common etiologic factor in this case She also has a patch of atrophy with telangiectasis on the lower lip which, I think, is an early necrobiotic lesion This disease usually occurs only on the shins, but lesions have been reported on various parts of the body

DR HAMILTON MONTGOMERY, Rochester, Minn Dr Hildebrand, Dr Ryneerson and I have recently reviewed 8 cases of necrobiosis lipoidica diabetorum observed in the clinic and analyzed them in relation to those reported in the literature, a total of 66 Addition of the 20 cases reported by Boldt (*Arch f Dermat u Syph* 179 74 [July] 1939) and referred to in this discussion by Oppenheim makes a total of 86 cases of this disease About 90 per cent of the conditions occur in women, and about 90 per cent are associated with diabetes In about 14 per cent of the cases the lesions of necrobiosis have appeared from one to five years before the onset of the diabetes In the cases of the 10 per cent of the patients who were regarded as nondiabetic there was frequently a history of diabetes in the family, and it is possible that the disease may eventually develop in them too Blood lipoids are not elevated, as a rule, unless the diabetes is severe In the nondiabetic patients there was no appreciable solution of the blood lipoids

DR MAURICE OPPENHEIM (by invitation), Chicago I am surprised to encounter here so many instances of the disease which I was first to describe There are more cases published in the United States of America than in all other countries together, then follow Germany and Italy I gave this disease the name "dermatitis atrophicans et necroticans lipoides diabetica" I published the first case in 1928 (*Wien klin Wchschr* 41 1490 [Oct 25] 1928), and Urbach followed me in 1932 (*Arch f Dermat u Syph* 166 273, 1932) and introduced the name "necrobiosis lipoidica diabetorum," because he noted lipid drops in the necrotic tissue I observed the lipid degeneration of the fibers of the connective tissue It has been made known by Unna that collagen if degenerated ends in amyloid and by Kreibich that in lipid too the elastin degeneration ends in colloid My opinion that in necrobiosis lipoidica there is a lipid degeneration of the collagen was accepted by Satenstein, Weidmann and others I differentiate the sharp, clearcut clinical features of the disease from other clinical pictures observed on the legs, mostly in women The opinion that traumatic lesions of the legs can lead to necrobiosis, as Michelson and Laymon suggested, I cannot accept There are three well defined stages of the disease (1) a hard red papule, (2) a red ring with a yellow center and (3) a central atrophy or necrosis so that target-like figures are the result In the last *Archiv fur Dermatologie und Syphilis* Boldt has published a survey of about 75 cases Forty-five cases are acknowledged, in 14 there was no evidence of diabetes The question arises whether diabetes is constantly present in all the cases Bottrow and Boldt stated the belief that the disease is caused by damage to the peripheral blood vessels, which is often observed in diabetes

I believe that some connection with diabetes is necessary in nearly all cases, though the connection may be occult Antidiabetic therapy, i e, restricted diet and insulin, has no good results

I should prefer the name "dermatitis atrophicans et necroticans lipoides diabetica" to "necrobiosis lipoidica diabetorum," because the disease starts with an inflammation and ends with lipid degeneration and necrosis

DR THEODORE CORNBLEET, Chicago I noticed the changes on the lower lip but did not regard them as being in any way due to necrobiosis I thought that they were manifestations of ordinary dermatitis Neither of the patients has diabetes Both had normal sugar tolerance tests In 1 case the lipoids were absolutely normal, in the other the cholesterol was elevated I think it is better

to make a fat tolerance test by giving a fatty meal, as demonstrated in both cases. There was intolerance for fat, whereas the carbohydrate metabolism was normal. Of course, in most cases of diabetes the fat tolerance is eventually altered. The patients probably have a potential diabetes. Changes in their fat metabolism and skin possibly forebode this. I believe that as time goes on the pathogenesis of necrobiosis may be found to be just as much dependent on the altered metabolism of fat as on that of the carbohydrates.

Scleroderma in a Chondrodystrophic Person Presented by DR THEODORE K LAWLESS, Chicago

A S, a boy aged 10 years, has had a progressive stiffness of the fingers and feet and patchy thickening of the integument for several years. Accompanying this has been a generalized hyperchondria with various areas of accentuation, thus resulting in a diffuse mottled appearance.

General physical examination shows chondrodystrophy, with generalized sclerodermatous lesions interspersed with pale to dull brown chronic areas. The face is thin and slightly marked. The alae nasi are thin, drawn and sclerotic. The chest is full, and the abdomen is enlarged, owing to a massive liver which extends about 4 fingerbreadths below the costal arch. The fingers are short, stiff and glistening. The bony and dermal structures of the feet are as though held in rigid tension.

The skin is mottled and taut, with patches of doughy consistency which are variable in size and shape. Over the joints the skin is thin. The normal markings are indistinct. There is no evident erythema, nor has atrophy been noted as yet.

The condition has shown some improvement from treatment with gonadotropic substance from the urine of pregnant women (antuitrin S) and an anterior pituitary extract containing the growth hormone (antuitrin G), oil massage and pancreatic extract.

DISCUSSION

DR PAUL A O'LEARY, Rochester, Minn. I had the opportunity of seeing this boy several months ago, and I felt that he had a chondrodysplasia of some type, essentially a dwarfism. In regard to his hands, I do not believe that every person who has a hardening of the skin of the hands necessarily has scleroderma. In many cases of so-called sclerodactylia, hardening of the skin of the fingers is a secondary phenomenon, not a part of scleroderma. I have in mind acrosclerosis and various types of arthritis of the hands in which there is an associated cutaneous sclerosis. The condition of the boy's hands has improved considerably in the last few months, probably as the result of the use of local heat and massage.

Kaposi's Sarcoma with Lesions of the Face Presented by DR ARTHUR W STILLIANS and DR E M SMITH JR (by invitation), Chicago

J A, a white man aged 72, has multiple small tumors of the face. About six years ago a large hard purple tumor mass was excised from the right side of the nose. Three years ago he noticed a small red area on each cheek, which developed rapidly into a dark reddish purple mass. At this time lesions also appeared on the right wrist and on the dorsum of the left hand. Some of the lesions are said to have cleared spontaneously.

General physical examination gave negative results for a man of his age.

Multiple vascular tumors several millimeters in diameter are distributed over the face. Two recently formed tumors, one at the base of the right nostril and the other under the left ear, were removed for histologic examination. The tumors were approximately 2 cm in diameter, were more rapidly growing and bled easily. One small lesion on the dorsum of one foot had not been noticed by the patient.

The Wassermann and Kahn tests gave negative reactions.

Histologic examination showed the main mass of the tissue to be composed of many angiomatous spaces, of which some were widely dilated and cavernous and others were in the papillary layer and characterized by being surrounded by a predominance of connective tissue. The connective tissue was adult in appearance in some areas, but in many others the cells were enlarged and the nuclei were large and granular, like those in fibroblasts. While no mitoses were seen, there was a tendency to whorl formation of the connective tissue in certain areas. There was a moderate amount of hemosiderin scattered through the tumor. It tended to be lobulated by dividing strands of connective tissue.

DISCUSSION

DR HARRY R FOERSTER, Milwaukee. The histologic observations support the diagnosis of Kaposi's sarcoma. Of special interest are the lesions on the face, an uncommon localization, and the numerous small nodular lesions.

A Case for Diagnosis (Dermatomyositis?) Presented by DR ARTHUR W STILLIANS and DR MAURICE DORNE (by invitation), Chicago

H G, a white man aged 66, a shoemaker, about eighteen months ago first noticed some slightly pruritic red spots on his arms and legs. Soon after this he noticed a puffiness of the face, muscular stiffness and later puffiness of localized areas on his feet and arms. Hospitalization and treatment on two occasions gave some relief for short periods, but with each relapse the puffiness and muscular stiffness involved more areas. Since the onset of the illness he has had two attacks of edema of the glottis that required emergency treatment. He had been well prior to this illness. Twelve years ago he had a tonsillectomy because of recurring attacks of tonsillitis.

He is a well nourished man, not acutely ill. There is puffiness of the eyelids, and the face is expressionless. He can open his mouth only partially and is unable to lift his tongue or to whistle.

Examination shows scaliness and redness of the scalp. The face and eyelids are dusky red and edematous. The chest, back and extremities are edematous. The smaller folds of the skin are lost. On palpation there is a solid nonpitting infiltration, and the skin is smooth. On the chest and back there is a diffuse dusky red macular eruption. On each ankle there is a circumscribed oozing and scaling patch. Some atrophy is noted of the shoulder and pelvic girdles.

Examination of the blood showed 2,800,000 erythrocytes and 9,950 leukocytes per cubic millimeter and 66 per cent hemoglobin. The color index was 1. Schilling's differential count showed 71 per cent segmented polymorphonuclears, no stab cells, 12 per cent eosinophils, 15 per cent small lymphocytes and 2 per cent monocytes. The basal metabolic rate was +17 per cent. Examination of the urine gave negative results. Chemical examination of the blood (whole blood) showed 32.8 mg of urea nitrogen, 67 mg of nonprotein nitrogen and 8.4 mg of calcium per hundred cubic centimeters. A culture of scrapings from the throat gave negative results. Culture of washings from the maxillary sinuses showed *Staphylococcus aureus*. The Wassermann and Kahn tests gave negative reactions. An electrocardiogram showed evidence of myocardial degeneration.

Roentgenographic study of the chest showed moderate widening of the left side of the heart and sclerosis of the aorta. Similar study of the sinuses showed chronic inflammatory changes over the maxillary and ethmoid cells.

Histologic examination of sections of skin and muscle showed the surface to be lined by a thin layer of hornifying stratified squamous cell epithelium. The papillary layer was atrophied. Beneath there was an increased amount of hyalinized connective tissue, which showed thickened capillaries and infiltrations with lymphocytes, fibroblasts and histiocytes, especially arranged around the blood vessels and the sweat glands. This infiltration was also present in the deeper areas. Another slide showed striated muscle, the cross striations of which were only partially distinct. Some of the fibers were swollen and homogeneous. In

some areas around the bundles there were infiltrations with lymphocytes and large mononuclear cells. The surrounding connective tissue showed the same granulation tissue as previously described.

The patient has received eight intravenous injections of typhoid vaccine in doses ranging from 12,500,000 to 75,000,000 bacilli at four day intervals. Improvement was evidenced by softening of the skin over the shoulders, chest and back, a lessening of the edema of the face and an increase in the mobility of the wrists and ankles.

DISCUSSION

DR PAUL A. O'LEARY, Rochester, Minn. I had the opportunity to observe this patient for several months beginning in July 1938, and to me the case is a striking example of the difficulty sometimes encountered in differentiating scleredema, dermatomyositis and acute edematous scleroderma. When I first saw the patient the evidence favored a diagnosis of acute scleredema. Dr. Montgomery interpreted the skin sections as manifestations of an acute scleroderma, but when the muscle tissue was studied the changes were compatible with dermatomyositis. The patient had a basal metabolic rate of +54 per cent, so he was given compound solution of iodine, although he did not present clinical evidence of hyperthyroidism and there was no evidence of localized myxedema. A considerable amount of the edema of the face and of the upper part of the trunk disappeared after several weeks' use of the compound solution of iodine. I thought today I saw more evidence of scleroderma of the arms than on any other previous occasion, and the patient said that this has become more pronounced in the past six months. Likewise, within recent months there has been recurrence of the edema of the face. The patient started out with a picture of scleredema of Buschke, was observed to have histologic evidence of a dermatomyositis and withering of the muscles of the shoulder girdle, which is a manifestation of dermatomyositis, and in addition he today shows definite evidence of linear scleroderma of both arms. As cases of this type have been studied during the past several years, I have felt that dermatologists were getting to the point where these conditions could be classified easily, but this patient disproves that, because he shows evidence of scleroderma, scleredema and dermatomyositis all at the same time. Today he also shows on the sides of the neck and on the upper part of the chest mottled areas of early atrophy, suggestive of early poikiloderma.

DR FREDERICK R. SCHMIDT, Chicago. I agree with Dr. O'Leary. Nevertheless, when one studies this group of dermatoses which is characterized by certain observations, one learns that there are certain experimental data which suggest that these dermatoses are disturbances not of metabolism but possibly of the circulatory system. In other words, certain conditions may be regarded as due to disturbances of the peripheral circulation. There are numerous cases cited in the literature to show that necrobiosis lipoidica, dermatomyositis, purpura annularis telangiectodes and erythromelalgia are associated with signs of oxygen deficiency. Other symptoms point to the supposition that these dermatoses are influenced by vascular spasm. Dr. O'Leary has reported several cases in which the condition was improved with oxygen therapy. I have patients in whom measures to promote vasodilatation have brought about considerable improvement in the condition.

DR HAMILTON MONTGOMERY, Rochester, Minn. I agree with Dr. O'Leary that this case is confusing because it presents features of all three diseases. For many years I have followed the histologic studies made of these conditions by various men that were in the department of dermatology at the clinic, including Dr. Nomland and Dr. Brock. Dr. Waisman has recently completed a thesis on dermatomyositis. I believe the typical forms of scleroderma adultorum, scleroderma and dermatomyositis can be distinguished histologically. In scleredema there is simply edema of the connective tissues, little infiltrate and no appreciable vascular changes. In scleroderma involving the skin, muscle or various internal organs, primary obliterative changes are observed about the vessels, and degeneration of

the muscle fibers is secondary to the vascular changes in the small interseptal blood vessels. In dermatomyositis one deals with a primary parenchymatous degeneration of the muscle bundles, including hyaline, vacuolar and granular degenerative changes. Rosenow has obtained positive cultures for streptococci in a couple of cases. Secondary calcification is observed in extensive cases of scleroderma but not as a rule in dermatomyositis.

DR CLINTON W. LANE, St. Louis. In the reports of many of the cases of early dermatomyositis it was stated that there was disturbance of the creatinine content. I should like to know whether a study has been made of the creatinine content in cases of acute scleroderma and dermatomyositis.

DR MAURICE DORNE (by invitation), Chicago. This patient was presented because of the difficulties encountered in attempting to classify his condition. After listening to Dr. O'Leary's remarks I feel that the combination suggested by him is the best theory presented thus far.

Pityriasis Rubra Pilaris Presented by DR S. W. BECKER and DR M. E. OBERMAYER, Chicago.

J. J., a boy aged 7 years, first came to the clinic on Aug. 29, 1939, because of a recurrent scaling eruption on his hands, feet, neck and elbows of eight months' duration. The eruption was first noticed in January 1939, as a redness and swelling of the hands and feet after the child had been playing in the snow. There was severe pruritus, and after three days the skin began to scale. His elbows and knees became affected in the same manner during the next ten days. The patient was treated by a physician in Evansville, Ind., with an ointment (type not known by the family), and all the lesions cleared in one week. Three weeks prior to admission the entire process recurred in the same areas and on the neck in addition. A decided thickening of the skin of the palms and soles was also noted.

The skin shows an erythematous scaling eruption with a yellowish tint over the neck, elbows, hands, ankles, feet and knees. Individual hyperkeratotic papules are noted about the follicles along the line of demarcation of the eruption. There are many small fissures over the extensor folds of the involved portions of the extremities and decided keratoderma of the palms and soles.

Examination of the blood and of the urine gave negative results. The Wassermann and Kahn tests gave negative reactions. The ascorbic acid content of the plasma during a period of fasting was 0.9 mg. per hundred cubic centimeters (within normal range). The basal metabolic rate was -5 per cent.

Histologic examination of a section from a diffuse plaque on the wrist showed a thick stratum corneum with some parakeratosis. The stratum granulosum was thickened and thinned irregularly, and one sweat pore showed hyperkeratosis. The epithelium was thickened, with many mitotic figures. The cutis showed minimal perivascular infiltrate, with vascular dilatation in its superficial portion.

A section from an isolated papule on the wrist showed enormous thickening of the stratum corneum, with irregular parakeratosis. The stratum granulosum was irregularly thickened. Hair follicles and sweat pores showed considerable hyperkeratosis. The papillae were somewhat edematous, with minimal round cell infiltrate in the superficial dermis.

DISCUSSION

DR MAURICE OPPENHEIM (by invitation), Chicago. This case is interesting to me. There has been some question as to whether pityriasis rubra pilaris and lichen ruber acuminatus were identical or not. The members know Devergie's statements. In 1889 Kaposi saw Devergie's patient, and expressed the opinion that the conditions in the 2 cases were identical. When I saw this boy with involution of the palms and soles and lesions on the forehead and on the chest, which were small, pinpoint-like nodules with hard thornlike scales in the center, I had the same impression.

DR S W BECKER, Chicago One reason we presented this patient was because the boy was sent to us some weeks ago from Indiana with lesions of the palms, soles and knees Some irritating or stimulating ointment had been applied The observations did not definitely lead to a diagnosis of pityriasis rubra pilaris Now some definite lesions of that disease have developed We have given him thyroid, which has been recommended by Zeisler (Zeisler, E P Pityriasis Rubra Pilaris—Familial Type, ARCH DERMAT & SYPH 7 195 [Feb] 1923)

**A Case for Diagnosis (Prurigo of Hebra? Pigmentation?) Presented by
DR S W BECKER and DR M E OBERMAYER, Chicago**

A S, a German mechanic aged 34, was first observed in the clinic on July 13, 1939, with a history of a cutaneous eruption over a period of nineteen years He first had pruritic "water blisters" between the fingers, which would persist for two to four weeks, break and leave reddened surfaces Some years later blisters began to develop between the toes and on the dorsa of the feet, which would become pustules and later form crusts Since May 1939 he has noticed many small pruritic papules in the flexors of his arms and knees and also an increased darkening of his skin His general health is good His past history and family history are not significant

Examination of the skin shows a generalized hyperpigmentation, with a brownish tint of the hair, as seen in Addison's disease The cervical, axillary and inguinal nodes are enlarged On the arms, forearms, upper part of the trunk and to a lesser extent the lower extremities are observed many flat-topped, angular, closely set papules, some of which show excoriations On the flexor surface of the fingers and palms are large patches of drying vesicles, and about the ankles a few crusted ulcers are noted

The Kolmer and Kahn reactions were negative The blood pressure was 120 systolic and 75 diastolic Examination of the blood showed 3,560,000 erythrocytes and 13,600 leukocytes per hundred cubic centimeters and 75 per cent hemoglobin The differential count showed 72 per cent polymorphonuclears, 14 per cent lymphocytes, 5 per cent monocytes, 8 per cent eosinophils and 1 per cent basophils The condition has shown little change under treatment

A microscopic section from a small papule showed the stratum corneum to be only slightly thickened The stratum granulosum was thickened irregularly The stratum mucosum was essentially normal except in the center, where it was slightly thin, and there was broadening of the papillae In this region the superficial cutis was involved in a moderate loose infiltrate composed of round cells and fibroblasts The superficial blood vessels were slightly dilated

DISCUSSION

DR FRANCIS E SENEAR, Chicago I realize that this case was presented with a question mark after the diagnosis, and I do not think that any one who has had experience in dermatology in this country only has observed enough cases of prurigo to have much confidence in his opinion, but I also think that there is nothing in this case that suggests a diagnosis of prurigo First, the condition is of relatively short duration in an adult, secondly, there are none of the individual small scratched papules, but there is rather a generalized eruption, and thirdly, the condition was much more intense in the cubital regions than either above or below The condition seemed to me to be a general lichenification Some kind of lymphoblastoma might be considered, although I appreciate the fact that there is nothing in the blood picture to suggest that background The case does not at all fulfil my conception of prurigo of Hebra

DR CLARK W FINNERUD, Chicago I observed a few cases of prurigo of Hebra in Vienna This condition has little resemblance to that in those cases My impression is that it is an excellent illustration of Dr Becker's own disease, a generalized neurodermatitis

DR MAURICE OPPENHEIM (by invitation), Chicago I observed many cases of Hebra's prurigo in Vienna In all the cases the condition started in infancy,

usually when the infant was taken off the breast and fed artificially. There is a difference between prurigo of the rich and prurigo of the poor. The poor are fed chiefly on potatoes and have a "potato prurigo," and the rich are fed largely on meat, it is the uniformity of the nutrition which causes the disease. On the other hand, prurigo is often associated with rickets, and it is believed that it is perhaps a hypovitaminosis. When children with the disease are admitted to the hospital the symptoms disappear spontaneously in a short time. When they return to their homes the symptoms reappear. There may be a want of sunlight too. Ultraviolet radiation is healing, and this was used for a long time before vitamin therapy was started and cod liver oil considered the best treatment. There is a difference also between prurigo mitis and prurigo ferox. The typical lesion of prurigo is round and yellowish-brownish, is better felt than seen and is located on the extensor sides of the extremities, especially the lower extremities, with thickening of the skin, lichenification and involvement of the femoral glands, this condition is called prurigo mitis. Owing to the scratching secondary infection, impetigo and eczema are observed. Impetigo and eczema are spoken of in pruriginoso, and these conditions are called prurigo ferox. The prurigo lasts from infancy until the age of 35 or 45 and then gradually disappears.

The condition in Dr. Becker's case does not give me the impression of prurigo. There is a rather high degree of general lichenification and glandular infiltration but no typical prurigo nodule, also, the fact that the disease started when the patient was 14 years old is against the diagnosis prurigo Hebra.

DR. S. W. BECKER, Chicago. The type of pigmentation and the generalized glandular enlargement were most interesting to me. I believe that the man has a peculiar dermatosis. He has large patches of vesicles on the palm. Patients with prurigo of Hebra are not seen in the clinic, but this condition is about as near to it. The blood count shows nothing typical of prurigo. I think the patient has generalized melanosis similar to that which occurs in prurigo of Hebra. The similarity is one reason we ventured this diagnosis. I do not believe that simple exposure to the sun around Chicago would account for so generalized a melanosis.

Acarophobia and Tumors Due to Camphor in Oil. Presented by DR. DAVID V. OMENS and DR. WALTER W. TOBIN, Chicago.

M. T., a woman aged 65, stated that since a sinus operation six years ago she has suffered from an intolerable pruritus all over her body and that by scratching or picking her skin she can remove insects or parasites. She has also recovered insects or parasites from her nose and from the stools and usually brings a collection on each visit. In 1917 after a serious abdominal operation she received injections of camphor in oil in her arms and thighs which formed lumps and scars, but these do not bother her.

Examination discloses an admixture of old scars and excoriations over the entire body which are more marked on the arms and shoulders. On the external surfaces of the arms and thighs are large areas of brownish yellow irregular firm keloidal nodules and contracted scars.

The Wassermann tests gave a negative reaction, and examination of the urine gave negative results.

The patient has been under treatment for three years and has even had neurologic therapy, but she has shown no improvement.

DISCUSSION

DR. RICHARD WEISS, St. Louis. The clinical picture of the tumors corresponds with Mook's original description (Mook, W. H. Camphor Oil Tumors, ARCH. DERMAT. & SYPH. 1.304 [March] 1920). The acarophobia is, of course, classic. It would be interesting to get sections of the tumors and check up with Mook's previous observations.

DR. MINNIE O. PERLSTEIN, Chicago. This woman was under my care for six years, during which time no treatment apparently improved her acarophobia.

phobia Her husband entered the hospital about three years ago with a similar condition The wife was committed to the psychopathic hospital, and the husband's symptoms cleared up while she was there, but as soon as she returned home he began itching again She told me today that he is still suffering from the "itch mites," although his condition is not as severe as hers

DR WALTER W TOBIN, Chicago No doubt the husband's pruritus is the result of association, since the condition improves when he is away from her The patient brings in alcoholic and aqueous preparations of parasites obtained from the nose and stools as well as from the skin

Parkes-Weber Syndrome Presented by DR FRANCIS E SENEAR, Chicago

C B, a boy aged 14, at birth had a number of dilated veins of the thighs, which were evidenced as bluish lines Gradually these enlarged until they became well developed varicosities Six to seven years ago it was noticed that a lesion was developing on the right sole and on the inner aspect of the right foot Soon after that the right great toe began to enlarge The growths involving the skin of the right foot have gradually increased in size, and enlargement of the bones of the right foot and leg has continued until the leg is now somewhat longer than the left About two and a half years ago the skin on the sole and sides of the left foot began to show the same changes that are present on the right foot

Physical examination shows a well developed boy with numerous varicose veins on both thighs The right leg is longer than the left, and the right foot, particularly the great toe, is larger than the left On the sole and lateral aspects of the feet are large, rather yellowish growths which are firm and present a cerebriform appearance

Roentgenographic examination of the right foot shows an irregular exostosis about the terminal end of the first phalanx of the great toe, with almost a complete ankylosis of the inner phalangeal joint The epiphysis on the first phalanx is almost closed All the bones of the great toe are considerably larger than the corresponding bones of the opposite foot There is also swelling of the soft tissue, involving practically the entire foot but most pronounced around the great toe The other bones of this foot also appear slightly larger than those of the opposite foot The changes in the soft tissues and bones are difficult to classify at this time

A section of tissue removed from the growth on the right foot was reported to show cornification of the epidermis and increased fibrosis of the subcutaneous layer

DISCUSSION

DR E M SMITH JR (by invitation), Chicago Here is a young boy with a varicosity of the leg, and I am wondering whether he has something more of a vascular condition inside the leg, such as nevi or arteriovenous aneurysms

DR WILLIAM ALLEN PUSEY, Chicago This case impresses me as one in which the specifications have not been well carried out in building the boy He has a congenital hypertrophy of one side If this is not a good name I should suggest that the condition be called "Senear's syndrome"

DR FRANCIS E SENEAR, Chicago At the clinical session of the American Dermatological Association, Inc, in Boston in 1936 (ARCH DERMAT & SYPH 35 727 [April] 1937) a patient with a condition designated as "Parkes-Weber syndrome" or hypertrophic hemangiectasia was shown The patient presented congenital varicosities, and later in life enlargement of the bones on the affected side developed In association with these changes, there is commonly present some type of nevoid change in the skin It is my understanding that the specialists in the neurocirculatory diseases do not accept this picture as a syndrome, since they observe so many variations, there being many instances in which the patients present only the congenital varicosities and the osteohypertrophy Likewise, the condition may be bilateral rather than unilateral The gradually developing bony hypertrophy is due to the overnourishment of the part from the excessive blood supply, since in these conditions there is basically an arteriovenous anastomosis

The dilated veins on the affected side are shown to contain a greater proportion of oxygen than the vessels on the opposite side. To dermatologists, of course, the cutaneous involvement present in some of the cases is the interesting feature.

Pigmentation (Fixed) Presented by DR THEODORE CORNBLEET and DR D COHEN, Chicago

J B, a Negress aged 35, first noticed a lesion on her nose during the summer of 1934. It was reddish and pruritic. Scratching increased the intensity of the redness, and quickly the lesion became darker. The patient insists that at that time she was not taking any drugs. Lesions continued to form on the nose during that summer. The following winter no new lesions erupted. During the next summer, however, other lesions again formed on the cheeks. With each succeeding summer new lesions have formed. They are now present on the nose, cheeks and dorsa of the forearms.

The lesions consist of half-dollar-sized deeply pigmented macules, with no inflammatory element. On the nose some areas show a retiform network. No decided subjective symptoms are present, and there is no history of drug ingestion.

Histologic examination shows only melanin to be present. There was no hemosiderin present.

DISCUSSION

DR RICHARD WEISS, St Louis. The most common opinion at first probably was that this condition is a healed lupus erythematosus, but on close examination there was none of the atrophic scarring usually seen after this disease, but merely pigmentation. If the present condition were limited to the face and did not appear on the arms, I should think it was possibly due to heavy metal, as described by Goeckerman, but this patient also has lesions on the limbs. I observed a case recently in which similar lesions were limited to the face, however, the patches were rather more diffuse. I was able to demonstrate by spectroscopic methods lead in fair amounts and mercury in rather large amounts. The patient had used cheap cosmetics of various kinds for many years. I wonder whether or not spectroscopic examination might show the presence of heavy metals as the cause of the pigmentation in this case.

DR THEODORE CORNBLEET, Chicago. I thought of lupus erythematosus as a background for this disturbance but could not substantiate that diagnosis. I have studied the possibility of drugs and worked along other lines without finding any real cause for the disease. The idea Dr Weiss presents is attractive. If the patient permits, some of her skin will be examined in the manner he suggested.

Parakeratosis Variegata (Lymphoblastoma?) Presented by DR S W BECKER and DR M E OBERMAYER, Chicago

C S, a man aged 34, was first seen in the clinic on April 7, 1934. He stated that he had had dry skin during his life but that what caused him to seek medical attention was an eruption which started when he was 12 years old as "thick" red pruritic patches. The lesions were limited to the extremities for the first five years and then gradually extended to involve the trunk.

General physical examination gave essentially negative results.

The eruption now involves the lower extremities, back, lower part of the abdomen and upper extremities. It consists of purplish scaling plaques, with some thickening. There is definite secondary infection, evidenced by pustules and crusting.

The Kolmer and Kahn reactions were negative. Examination of the urine gave negative results. The blood lipids were within normal range.

A diagnosis of parakeratosis variegata was made, and the patient was presented at a meeting of the Chicago Dermatological Society (ARCH DERMAT & SYPH 30 755 [Nov] 1934), and the diagnosis was concurred in. He was treated with ointment of coal tar, ultraviolet rays, autohemetic therapy and a low protein diet, with some improvement. He was lost from observation in December 1934.

The patient returned on Aug 24, 1937, and presented a somewhat different picture. He had been at the Mayo Clinic, where a diagnosis of lymphoblastoma was made. The eruption had become more generalized, and there was extensive atrophy of the skin, with some pigmentation and telangiectasia, especially on the extremities. On the trunk there were still many areas of scaling resembling those of parakeratosis variegata. Numerous furuncles were present on the trunk and extremities, with a tendency to appear only in areas not tanned by the sun. In many areas the signs were those observed in poikiloderma.

Treatment was started with ammoniated mercury ointment, ultraviolet rays and staphylococcus toxoid. A test dose of the last gave no reaction whatever. The patient failed to return after the second injection.

A microscopic slide by Dr Hamilton Montgomery showed the stratum corneum to be somewhat thickened, with a few areas of parakeratosis. The stratum granulosum was alternately thickened and thinned. The stratum mucosum was thickened in some places and in others was thinned down to three layers of cells. An abundant infiltrate was present in the superficial dermis, extending along the blood vessels somewhat more deeply. The infiltrate consisted of lymphocytes and fibroblasts, was rather loose and appeared to be edematous, and there were many newly formed blood vessels. Some of the deeper blood vessels showed thickening of the wall, about which were many eosinophilic mononuclear cells.

DISCUSSION

DR HOWARD J PARKHURST, Toledo, Ohio: This pruritic poikiloderma-like eruption impressed me as one which might eventually prove to be a lymphoblastoma of the mycosis fungoides type.

DR HAMILTON MONTGOMERY, Rochester, Minn.: When I saw this patient at the Mayo Clinic the histologic picture was a specific one of lymphoblastoma, although the type of lymphoblastoma could not be diagnosed. The most difficult histologic diagnosis that I have to make is to decide in regard to early lymphoblastoma. In the past I have erroneously diagnosed generalized neurodermatitis or atopic eczema, in which the infiltrate may be dense, as probable early lymphoblastoma. On the other hand, I have observed cases of extensive atopic dermatitis, conditions which histologically I regarded as definite lymphoblastoma but which cleared up promptly under treatment, only to recur a year or two later presenting the features of mycosis fungoides. I believe that lymphoblastoma of any type may start as a benign inflammatory dermatosis, and only as the result of prolonged and chronic irritation over a period of months and years develop eventually into one of the lymphoblastomas. Whether mycosis fungoides, Hodgkin's disease and the leukemias are regarded as true malignant neoplasms or not, the eventual prognosis is death.

CLEVELAND DERMATOLOGICAL SOCIETY

C. L. BASKIN, M.D., *President*

C. G. LAROCO, M.D., *Secretary*

JAMES R. DRIVER, M.D., *Reporter*

Sept 28, 1939

Granuloma Annulare, Advanced Bilateral Cavitating Pulmonary Tuberculosis Presented by DR HAL E. FREEMAN

J. T., a man aged 36, presented from the Tuberculosis Division of the Cleveland City Hospital, has been under treatment for advanced cavitating pulmonary tuberculosis for several months.

An eruption started in April 1939 and has continued with alternating periods of improvement and exacerbation. Symmetrically and diffusely distributed over the upper extremities, back, chest and thighs is a purplish red eruption consisting of numerous circinate lesions. Some of the lesions are annular, while others are half-moon shaped or polycyclic. All have palpable, slightly raised borders.

A roentgenogram of the chest revealed a dense mottling throughout the upper lung fields and at the level of the sixth interspace bilateral tuberculous cavitation.

Serologic tests for syphilis gave negative results. Sputum stained for tubercle bacilli was positive.

Histologic examination of tissue showed mild hyperkeratosis, some parakeratosis and two small epidermal abscesses. There was moderate acanthosis, and in the upper part of the corium several accumulations of cells were observed, most of which were epithelioid cells and a few of which were lymphocytes. Some of the accumulations were perivascular, but most of them were located in lymphatic spaces. No giant cells or tubercle bacilli were observed in appropriately stained sections.

DISCUSSION

DR HAROLD N. COLE: I think this condition is the most extensive example of what is apparently granuloma annulare that I have ever observed. Ordinarily one expects to find lesions on the hands or perhaps on the legs in this disease, but this patient has lesions distributed over his extremities and his trunk as well, and apparently they are characteristic lesions. Moreover, a picture of this sort in a patient who has true tuberculosis is also interesting. The possibility of the relation between granuloma annulare and tuberculosis is constantly mentioned, and here is a man with tubercle bacilli in his sputum and many examples of the former disease. I think it would be well worth while to look for organisms in the local lesions.

DR HAL E. FREEMAN: No organisms were found in sections stained for tubercle bacilli.

DR C. L. BASKIN, Akron, Ohio: There are so many lesions covering so much of the body that I am inclined to doubt the diagnosis. The large amount of involvement, practically the whole body, seems peculiar to me.

Localized Amyloidosis Cutis (Lichenoid Type) Presented by DR GERALD DEOREO

J. H., a man aged 48, presented from the Department of Dermatology and Syphilology of the Cleveland City Hospital, has been observed in the outpatient department since 1933 because of myocardial failure due to diffuse vascular disease. For the past two years he has been aware of a moderately pruritic, progressive eruption on the anterior surface of both legs. General physical examination gave negative results. There was no evidence of systemic amyloidosis.

On the anterior surfaces of both legs are numerous, bilaterally symmetric, well defined, papular lesions. Individual papules are 1.5 to 2.5 mm in diameter and are firm, pale reddish brown and surrounded by normal epithelium.

Congo red, 1 cc of a 15 per cent solution, was injected intracutaneously, the area was observed for seventy-two hours but showed no change in color. Urinalysis and a hemogram were normal. Serologic tests for syphilis gave negative results.

Histologic examination of tissue showed in the center of the section that the papillae were greatly thickened and the overlying epidermis was thin, with

moderate hyperkeratosis. At the margin the papillae were elongated and irregular. The swollen papillae contained collections of pale pink-stained hyaline material, between which were numerous young capillaries. The hyaline material did not give a positive Benneholdt reaction. In the deeper part of the corium, particularly beneath the lesion, the blood and lymph vessels were surrounded by fuzzy collars of lymphocytes and large mononuclear cells.

DISCUSSION

DR EARL W. NETHERTON: I agree with the diagnosis as presented.

DR C. B. NORRIS, Youngstown, Ohio: Was the congo red injected into the lesions?

DR GERALD DEOREO: It was injected immediately into a group of lesions, both subcutaneously and intradermally.

DR J. E. FISHER: I favor the diagnosis as presented. I once presented a patient with lesions similar to this, and a diagnosis was made of lichen planus ocreaformis of Lieberthal. There is a picture of this condition in Sutton's textbook (Sutton, R. L. *Diseases of the Skin*, St. Louis, C. V. Mosby Company, 1931, p. 197).



Localized amyloidosis cutis (lichenoid type)

DR H. J. PARKHURST, Toledo, Ohio: I think the eruption in this case corresponds to lichen planus ocreaformis (Lieberthal), although the appearance of the section substantiates the diagnosis of amyloidosis.

Argyrosis Presented by DR HAL E. FREEMAN

J. S., a man aged 69, has been admitted to the Cleveland City Hospital on five different occasions in the last three years because of a severe hypertensive cardiovascular disease with decompensation. He was presented previously before the society (*ARCH. DERMAT. & SYPH.* 37:327 [Feb.] 1938). He is presented today because of the pathologic pigmentation which followed the use of "two or three" bottles of 20 per cent silver nitrate over a period of two years prior to 1936. The medication was painted on the tongue in the treatment of leukoplakia, which was thought to have followed excessive smoking.

The face, scalp, neck and trunk are evenly and diffusely pigmented a grayish, ashen blue color which has on occasions been confused with cyanosis. There is a violet-silver line at the gingival margins.

Serologic tests for syphilis gave strongly positive reactions. No antisyphilitic treatment has been given.

Histologic examination of the skin revealed silver pigment in the basal cells and in the connective tissue of the corium, especially about the sweat glands. Examination of tissue removed from the tongue showed a lymphocytic infiltration and silver pigment in the epithelium and in phagocytic cells in the deeper layers.

DISCUSSION

DR E J ARDAY, Lakewood, Ohio. I believe it is a well known fact that argyrosis cannot be produced locally unless there is access to the alimentary canal. Silver preparations used as nose drops or painted locally in the nose, mouth or nasopharynx most commonly result in this disease.

DR C L BASKIN, Akron, Ohio. I believe that I may have produced conditions of that kind several times many years ago by administering silver arsphenamine.

DR HAL E FREEMAN. I should like to ask whether if a person is highly susceptible to one heavy metal he is susceptible to another. I contemplate using bismuth and mercury in the treatment of syphilis in this patient.

DR HAROLD N COLE. I do not think that there is any relation in the least.

DR EARL W NETHERTON. Argyria is not a sensitization to silver. It is a deposit of a silver salt in the skin.

DR BENJAMIN LEVINE. In one patient I was able to make the pigmentation disappear in areas into which sodium thiosulfate was injected.

DR E J ARDAY, Lakewood, Ohio. I think that sodium thiosulfate will produce the pigmentation again.

DR JAMES R. DRIVER. To my knowledge no evidence has been produced to prove that sensitization is a factor in this condition. Apparently argyria may develop in any one by whom enough of a silver salt has been absorbed, either from the gastrointestinal tract or from any other mucous surface. Cases have been reported in which the absorption resulted from urethral injection of silver compounds.

DR JOHN E RAUSCHKOLB. According to qualitative chemical analysis, the ions of silver, mercury and lead unite with the chlorides to form the insoluble chlorides. Since there is almost always free hydrochloric acid in the stomach, may not the silver salts, which are ingested but dissociated and formed into silver chloride, be carried by the blood stream and be deposited in the skin? The development of argyria, I believe, is a photosensitive phenomenon, such as takes place in photography. Any of the silver halogens, of which the chlorides are a part, are photosensitive.

A Case for Diagnosis (Keratosis Blennorrhagia?) Presented by DR HAL E FREEMAN

D F, a Jew aged 23, has been in the Cleveland City Hospital since January 1937 for treatment of severe atrophic arthritis involving the spine and most of the joints of the extremities. In July 1937 a widespread eruption developed, which was diagnosed as psoriasis. There was no involvement of the head or neck. He stated that he had not had gonorrhea. At the present time the spine is fixed, and the knees, hips and shoulders show marked limitation of motion. The fingers are flexed and also show limited motion.

Widespread over the body excepting on the head and neck is a hyperkeratotic pustulosquamous eruption. Individual lesions vary from the size of a pea to that of a half-dollar. The nails are thick, dull yellow and friable. The lesions do not favor the extensor surfaces as they commonly do in psoriasis.

The hemogram was normal. Serologic tests for syphilis gave negative results. Urinalysis and prostatic smears revealed no gonococci.

The patient has received various types of treatment for arthritis, including sixty-nine mechanofever treatments and sixty treatments with iontophoresis and mecholyl (acetylbetamethylcholine hydrochloride), without appreciable improvement.

Histologic examination revealed hyperkeratosis, parakeratosis and acanthosis. The outstanding characteristic was a large number of epidermal abscesses. They were larger than the minute abscesses of Monro and resembled more those observed in keratosis blennorrhagica.

DISCUSSION

DR H J PARKHURST, Toledo, Ohio. A diagnosis of keratosis blennorrhagica is not probable, since there is no evidence of a gonococcic infection from either the history or the examination. The patient stated that he had what was called psoriasis a year or so ago. The present cutaneous lesions correspond to those I have noticed on several occasions in patients with polyarthritis and which I have classified as pustular bacterid or pustular psoriasis. Many lesions of this type correspond closely to those of keratosis blennorrhagica. They may be of similar origin.

DR HAROLD N COLE. There are some reports of cases of arthropathies in which lesions resembling keratosis blennorrhagica are observed and in which there is no gonococcic infection. I think that the possibility of this condition's being an arthropathy should be considered. The lesions are rather waxy, have a tendency to be slightly crusted, and pile up in the same way as in keratosis blennorrhagica, and there are changes in the nails like those in psoriasis.

DR HAL E FREEMAN. Histologically the picture is not that of psoriasis. There are intraepidermal abscesses, but they are large, not like those described by Monro. The whole picture is that of hyperkeratosis and parakeratosis, with large abscesses like those seen in keratosis blennorrhagica, in spite of the absence of a gonorrheal infection in the patient.

NOTE—Dr Freeman, at the October meeting of the society, stated that he favored a diagnosis of keratoderma associated with atrophic arthritis instead of psoriasis for the following reasons. The scalp has always been clear, the blood cholesterol has been low (80 mg per hundred cubic centimeters) and there has been no pitting of the nails. According to the last article by Epstein (Epstein, E. Differential Diagnosis of Keratosis Blennorrhagica and Psoriasis Arthropathica, *ARCH DERMAT & SYPH* 40 547 [Oct] 1939), keratosis blennorrhagica responds satisfactorily to fever therapy, which this patient has had a great deal of. If that statement is true, gonorrheal keratoderma could be ruled out.

Rosacea-Like Tuberculid of Lewandowsky, Pulmonary Tuberculosis Presented by DR HAL E FREEMAN

M T, a woman aged 43, has had an eruption on the face associated with weakness and loss of weight for six months. Distributed chiefly over the forehead, nose and cheeks are numerous papular lesions of various sizes which are discrete, rather flat and dusky red or brownish.

Roentgenograms revealed an active bilateral cavitating pulmonary tuberculosis. Tubercle bacilli were demonstrated in the sputum.

DISCUSSION

DR EARL W NETHERTON. What was the result of the tuberculin tests?

DR HAL E FREEMAN. The patient is shown through the courtesy of the tuberculosis division of the Cleveland City Hospital, and tuberculin tests are not performed on these patients.

DR EARL W NETHERTON. According to the cases reported by MacKee and Sulzberger (*ARCH DERMAT & SYPH* 31 159 [Feb] 1935), patients with this condition are supposed to be sensitive to tuberculin in great dilutions.

DR HAROLD N COLE It seems to me that the diagnosis is consistent, and in this case it is known that the patient has tuberculosis

DR JAMES R. DRIVER It may be well to emphasize that this disease should be called rosacea-like tuberculosis It is histologically a true tuberculosis of the skin and not a tuberculid

Subcutaneous Fat Necrosis of the Newborn (Obstetric Lipophagic Granuloma). Presented by DR H H JOHNSON

C M, a Negro boy aged 6 weeks presented from the Department of Dermatology and Syphilology, through the courtesy of the department of pediatrics, the University Hospitals, at the age of 1 week had a firm nontender area, 10 by 6 cm, on his back The mass was slightly raised, and the overlying skin was moderately hyperpigmented

On palpation the subcutaneous tissue is firm and rubbery and is made up of several irregular nodules There are several smaller similar lesions, 1 cm or more in diameter, situated over the lateral aspects of both arms The skin otherwise is normal in appearance

General physical examination revealed nothing abnormal The hemogram was normal Tuberculin tests gave negative results The calcium content of the serum was 10.5 mg per hundred cubic centimeters, the phosphorus content 6.6 mg, the cholesterol content 113 mg and the protein content 6.25 Gm Calcium deposits could not be demonstrated by means of roentgenograms

Histologic examination showed skin which was covered with an intact layer of stratified squamous epithelium, the basal layer of which contained considerable pigment There were numerous sweat glands and sebaceous glands, as well as hair follicles In the subcutaneous tissues there were foci of fat necrosis, which were surrounded by great numbers of foreign body giant cells, lymphocytes and plasma cells In these areas there was also considerable fibrosis

DISCUSSION

DR JOHN A GAMMEL I certainly appreciate seeing this rare condition It is the first example I have seen

DR HAROLD N COLE I have been in consultation on several cases of this condition in the pediatrics divisions of the University Hospitals This manifestation is generally on the back, but it is sometimes observed on the outside of the arms, occasionally over the thighs and now and then over the chest The explanation that is given is that the babies are slapped vigorously at birth in order to get them to breathe, and this trauma produces the lesions The process lasts from a few weeks to a few months before it gradually disappears Histologic examination reveals a peculiar fat necrosis Fat stains show all these areas to be infiltrated with deposits of fatty crystals The disease must be differentiated from sclerema of the newborn in which a child with severe malnutrition is concerned In sclerema of the newborn the tissues become so hard that the child often is unable to open the mouth or flex the limbs

Angioma Serpiginosum. Presented by DR HAROLD N COLE and DR J R DRIVER

M L, a woman aged 43, four years ago noted an unusual increase in redness of the arms A similar change had been noted on her legs three years previously.

On the arms, but more decidedly on the legs, is a diffuse erythema consisting of many minute dilated superficial capillaries Many of the vascular areas show an annular arrangement with a central area suggesting atrophy Here and there on the areas bright red puncta are seen

The hemogram was normal Serologic tests for syphilis gave negative results

Histologic examination showed a few superficial capillaries in the upper part of the corium just beneath the epidermis There was no evidence of hemorrhage

DISCUSSION

DR EARL W NETHERTON I agree with the diagnosis as presented. On careful inspection of the arms areas are observed which look like little circular lesions formed by telangiectases. The interesting thing is that the manifestations disappeared rather quickly and all at the same time. The patient told me that the disease developed rapidly. There is no atrophy or scaling, such as in poikiloderma.

DR H A HAYNES JR, Akron, Ohio I have had a patient with angioma serpiginosum who showed great improvement after ultraviolet irradiation.

MANHATTAN DERMATOLOGIC SOCIETY

GEORGE C ANDREWS, M D, *President*

ANTHONY C CIPOLLARO, M D, *Secretary*

Oct 10, 1939

Parapsoriasis Presented by DR FRED WISE

F B, a woman aged 38, under the care of Dr Frances Pascher at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, presents an eruption which first appeared in April 1937 on the inner aspect of both arms, with a gradual increase in the number of lesions. Lesions on the thighs and ankles appeared shortly after. Symmetric involvement of the upper and lower extremities has been a striking feature since the start. The lesions are round and oval, noninfiltrated, lentil-sized to pea-sized, pinkish macules, covered with scales. Those on the inner aspect of the arms, near the axillas, are most pronounced. They do not itch.

The histologic examination by Dr David L. Satenstein confirmed the clinical diagnosis of parapsoriasis.

Since the onset there has been no change in the character of the lesions, and none of them have shown a tendency to recede. Coincidental with the onset of the eruption, a fever developed, with variation from 99 to 101 F and occasionally to 103 F. Investigation failed to disclose the cause of the fever. The patient also suffered from cystic mastitis.

The reactions to a Mantoux tuberculin test with a dilution of 1 1,000,000 was plus-minus, with a dilution of 1 10,000, 2 plus, and with 1 5,000, 3 plus.

DISCUSSION

DR MAX SCHEER I agree with the diagnosis only because the histologic picture confirms it. Clinically I could not make a diagnosis in this case.

DR WILBERT SACHS I think that this condition is parapsoriasis. It is superficial, and there is a slight scale. It is of two years' duration and has not changed.

Urticaria Pigmentosa Presented by DR FRED WISE

J M, a boy aged 2 years, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Sept 28, 1939. He presented a generalized eruption which had appeared several months after birth.

The neck and almost the entire trunk, front and back, are studded with numerous, closely crowded, yellowish brown lesions. Those on the neck are flat and from the size of a lentil to that of a dime, those on the trunk are elevated and somewhat infiltrated and vary in size from 2 to 10 cm in lengthwise diameter. The larger plaques present faintly depressed midportions of light yellow, while their peripheries are brown. Itching is entirely absent, and there are no signs of spontaneous urticaria.

Rubbing some of the lesions causes them to swell and become red.

The histologic examination by Dr David L. Satenstein showed the typical changes of urticaria pigmentosa

DISCUSSION

DR GEORGE C. ANDREWS Frequently in discussions of urticaria pigmentosa at medical meetings failure to produce urtication is emphasized as evidence against the diagnosis. In this case Dr Wise was able to demonstrate this sign only two or three times.

DR PAUL E. BECHET I do not believe that the color of the lesions is of much diagnostic value. I have observed many cases in which the lesions were dark brown to brownish black and others in which the color was almost that of xanthoma. That the latter condition is not uncommon is well known, as one of the synonyms of urticaria pigmentosa is xanthelasmaidea.

Hereditary Trophedema (Milroy-Meige Disease) of the Extremities Associated with Ptosis Palpebrae in Three Generations Presented by DR DAVID BLOOM

A C, a white man aged 39, was born of Russian Jewish parents. Except for having recurrent furunculosis he has been in good general health and attends without difficulty to his occupation as electrician. The swelling of his ankles and legs started when he was 16, and ptosis of his left upper eyelid has been present as long as he can remember, probably since birth. While the edema of the legs used to disappear after a night's rest in bed, the edema of the ankles has receded only slightly. For about eight years after the appearance of the edema the patient had recurrent attacks of inflammation of both legs, which was diagnosed by the attending physician as erysipelas but which is inferred, from the description, to have been lymphangitis. The attacks started with pain in the groin and were associated with chills and high fever. They occurred two or three times a year and ceased entirely about fifteen years ago. The degree of the swelling has not changed in the last few years.

Examination after the patient has been on his feet for many hours shows only moderate edema of the legs but a padlike thickening over the ankles. The ankles feel soft and show slight pitting on pressure. The feet and toes look thickened, and there is some verrucous formation on the dorsal surfaces of the toes. Maceration of the skin in the webs of the toes is due to dermatophytosis.

Numerous members of the family are also affected with edema of the ankles and legs but to a much greater degree, and they also show ptosis of the eyelid. The affected members are his younger brother, his father, an aunt (the father's sister) and his grandfather. Every family member affected with edema has ptosis of the left upper eyelid, and his aunt has ptosis of both upper eyelids. His grandfather has considerable involvement of only one leg, while the other leg is only slightly affected. All the other affected members of the family have involvement of both legs and both ankles of equal intensity. Edema started in the affected family members when they were between the ages of 12 and 16. The patient's younger brother gave a history of recurrent attacks of lymphangitis of the lower extremities which occurred once or twice a year. The father stated that his recurrent attacks of lymphangitis stopped when he was 20. A cousin of the patient (the son of his father's brother), aged 18, has no edema of the legs but shows ptosis of the right eye, his parents and his 3 sisters are normal, according to his statement.

This pedigree shows that among 21 relatives (13 males and 8 females) in three generations, 6 are affected with both trophedema and ptosis of the eyelid, while 1 show only ptosis. Five members of the second generation who died in infancy or in childhood and 3 members of the third and 4 of the fourth generation who are still infants or of childhood age are therefore not included in this count.

DISCUSSION

DR DAVID L SATENSTEIN According to his history the patient had a fever and lymphangitis. These observations do not belong to trophedema and ptosis. Furthermore, Dr Bloom stated that the patient had dermatophytosis of the toes, which should be sufficient to account for the lymphangitis.

DR WILBERT SACKS Milroy's disease not only is familial but is present at birth or shortly after. The dermatosis in these patients developed much later in life. The incidence of Milroy's disease is much higher in females, the opposite is true in this series. In Milroy's disease the legs and even the entire lower extremities are involved, in this series the edema is found no higher than the ankles except in 1 case. In Milroy's disease the edema is persistent and is not relieved by a change in posture, in these patients the edema is intermittent and can be relieved by a change in posture. There may be some other congenital anomaly, such as a polycystic or horseshoe kidney, to account for the clinical picture here presented.

DR GEORGE C ANDREWS There is no known connection between the ptosis of the eyelids and the enlargement of the leg.

DR GEORGE M LEWIS Because of the fever and the lymphangitis, I wonder if any bacteriologic studies were made. Some patients have both fungi and streptococci between the toes, and there is always a question as to the cause of the lymphangitis. It might be of some importance to determine the exact mycologic and bacteriologic flora of this patient's feet.

DR ISADORE ROSEN I believe that the thyroid and the pituitary should be studied in this case, because abnormalities of this nature are sometimes associated with disturbances of these glands.

DR DAVID BLOOM Attacks of inflammation of the legs accompanied by chills and fever occur frequently in cases of Milroy's disease. I obtained a history of these observations in each of the 3 cases I examined. I also found a report by Hope and French in 1907 (*Quart J Med* 1 312, 1907) which mentioned the occurrence of these attacks in most of their patients. The dermatophytosis of the toes probably favors a diagnosis of streptococcic infection of the legs. The regularity and frequency of the attacks are explained by the presence of lymphedematous tissue.

It is true that in 21 of the 22 cases of Milroy's disease the condition was congenital, but in the cases reported a few years later by Meige the edema developed at puberty. In none of the cases reported by Hope and French was the condition congenital, instead it developed in infancy, during childhood or in early adult life. Both the congenital and the tardive form are hereditary. Thus all the examples may be included under the name Milroy-Meige disease. Although the analysis of recorded families may indicate more affected females than males, which is possibly due, according to Cockayne, to the presence of another gene in the sex chromosome, the number of cases is perhaps too small to show a real preponderance of females. The number of families reported may be, as far as I can judge from a superficial survey of the literature, close to twenty.

The peculiarity which this pedigree presents is that the trophedema is associated with another hereditary abnormality, namely, ptosis of one or both eyelids. The fact that the trophedema is considered a disturbance of the vasomotor nerve and is associated with a definite nerve disturbance is significant. This and the fact that one member of the family showed only ptosis of the eyelid and not the edema of the extremities yields possibly good material for speculation on the hereditary mechanism in familial cases.

Purpura Simplex Presented by DR ANTHONY C CIPOLLARO

F D, an electrician aged 44, was first observed at my office on April 4, 1939, at which time he had an eruption involving the upper and lower extremities of

ten days' duration He attributed his condition to contact with rat poison used on electric cables The patient had no gastrointestinal disturbance, pains in the joints or hemorrhages from the mucous membranes at the onset of the eruption but now complains of pains in the ankles, knees and elbows and also of general malaise

The patient now presents purpuric lesions in different stages of involution and evolution, affecting the lower extremities, hips, abdomen and forearms The physical examination gives negative results other than edema of the ankles The spleen, liver and lymph nodes are not enlarged His teeth are loose and in poor condition The character of the eruption changes from day to day The blood pressure is 130 systolic and 76 diastolic

The tourniquet test gave negative results after fifteen minutes The moccasin venom test with a dilution of 1:3,000, showed after one hour a central purpuric area measuring approximately 0.5 cm and a surrounding area of edema about 5 cm in diameter, which after a few hours became purpuric

The patient is now receiving moccasin snake venom subcutaneously, calcium gluconate by mouth and citrus fruits

Examination of the blood gave the following results

| | |
|---------------------------------|--------------------------------|
| Hemoglobin | 85 per cent |
| Red blood cells | 4,500,000 per cubic millimeter |
| White cells | 7,900 per cubic millimeter |
| Color index | 0.94 |
| Coagulation time (Lee's method) | 10 minutes |
| Venous blood | 5 minutes |
| Capillary blood | 3 minutes |
| Bleeding time | 120,000 per cubic millimeter |
| Blood platelets | |

A differential count gave the following results

| | |
|--|---------------|
| Polymorphonuclear neutrophils (filamented) | 77.5 per cent |
| (nonfilamented) | 2.5 per cent |
| Small lymphocytes | 16.5 per cent |
| Monocytes | 2.0 per cent |
| Eosinophils | 1.5 per cent |

DISCUSSION

DR GEORGE C ANDREWS It seems to me that, judging from the blood count, it is better to make a diagnosis of thrombopenic purpura than of purpura simplex. The patient has distinct pharyngitis which should be treated

DR FRED WISE If snake venom were not used, what treatment would you give this patient, Dr Cipollaro?

DR ANTHONY C CIPOLLARO I think that the condition is purpura simplex. I have not been able to determine the cause, and as in so many cases, the cause may never be determined. There is probably some focus of infection. There is no definite evidence that the cause is poisoning with a heavy metal. Nevertheless, the history of contact with rat poison has to be taken into consideration. The diagnosis of thrombopenic purpura was not made because there is only the slightly lowered platelet count to substantiate that diagnosis. There has never been free bleeding from the gums. I do not know of any specific treatment for this condition. Most patients recover, especially if the condition is of infectious origin.

A Case for Diagnosis (Lupus Erythematosus?). Presented by DR MAURICE J COSTELLO

B S, a woman aged 51, states that the condition began on July 6, 1938. A papule appeared on the tip of the nose and attained the size of a nickel in several

months On the bulbous portion of the nose is a lesion which is crusted and sharply demarcated, and in the suboccipital region is another which is silver dollar-sized, well circumscribed and erythematous, with diffuse thinning of the hair Recently a number of slightly scaly large papules have appeared on the backs of the hands and wrists

She has received ten fractional doses of unfiltered roentgen rays on these areas and about twelve intravenous injections of gold sodium thiosulfate in doses of 10 to 50 mg, without benefit She was also given 0.32 Gm (5 grains) of sulfanilamide three times daily for two weeks, without visible effect

The Wassermann reaction was negative The heart and lungs are normal She has a history of allergy and has suffered from asthmatic attacks for a number of years The blood sugar was 110 mg per hundred cubic centimeters Her blood count showed 5,040,000 erythrocytes and 7,300 leukocytes per cubic millimeter and 80 per cent hemoglobin The differential count showed 39 per cent polymorphonuclears, 47 per cent lymphocytes and 14 per cent eosinophils The urine showed a faint trace of albumin

DISCUSSION

DR PAUL E BECHET I believe that the lesion on the nose is lupus erythematosus It belongs to that variety of lupus erythematosus which presents thickened infiltrated hypertrophic plaques, with cribriform atrophy The patch on the occipital region is superficial, reddened and covered with loose scales and presents no atrophy It closely resembles circumscribed neurodermatitis, which is so common in that location in women

DR ANDREW J GILMOUR I believe that the eruption on the back of the neck is seborrheic eczema which has been modified by rubbing, and the lesion on the nose I accept as lupus erythematosus

DR FRED WISE The fact that this patient has stippling of the nails leads one to suspect that the lesions on the face and scalp are an unusual manifestation of psoriasis

DR GEORGE C ANDREWS The patient looks sick I think she has a nutritional deficiency The tongue appears atrophic and glazed I have observed 1 case in which there was neurodermatitis on the back of the neck, and the condition was cured by nutritional therapy I suggest that a blood count be made and injections of a liver extract be given, also the patient should be placed on a high vitamin diet I think the best diagnosis is lupus erythematosus, with stippling of the nails of unknown cause, but I believe that there are many kinds of lupus erythematosus and that the condition in this case is nutritional in origin

DR MAURICE J COSTELLO This eruption has the clinical features of both lupus erythematosus and seborrheic eczema Its resistance to treatment favors the former diagnosis

Basal Cell Epithelioma? Presented by DR E WILLIAM ABRAMOWITZ

C K, a girl aged 23, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in October 1939, with a lesion on the cheek which is of fifteen years' duration and has not changed since it became well developed, which was when she was 8 years old

The lesion is situated on the right cheek and is the size of a split pea It is depressed, and along the periphery are tiny waxy nodules On superficial examination it has the appearance of a basal cell epithelioma

DISCUSSION

DR J FRANK FRASER This lesion is an epithelioma, probably belonging to the variety which arises from the appendages What structures are involved,

whether they are sweat ducts or hair follicles, can be determined only by microscopic examination

DR. ANTHONY C. CIPOLLARO The patient came to the clinic to have a wart on the finger removed. The lesion on the cheek was seen by the examining physician. The depression and the definite waxy nodules along the periphery suggested the possibility of an epithelioma of the basal cell type, as well as trichoepithelioma or benign cystic epithelioma.

DR. FRED WISE I agree with Dr. Fraser that the lesion is probably an epithelioma having its origin in the sweat ducts.

DR. DAVID BLOOM I agree with the diagnosis of basal cell epithelioma. I think that basal cell epitheliomas of this type are not rare in young persons.

DR. WILBERT SACHS I agree with Dr. Fraser, but I would rather call the lesion a nevoid type of epithelioma, similar to trichoepithelioma. I believe that it belongs to the nevus group rather than to the usual type of epithelioma. If it involves the sweat glands it is an adenoma, if it involves the hair follicles it is an epithelioma of the nevus type.

DR. PAUL E. BECHET To my mind there are important reasons other than the age of the patient and the long duration of the lesion which can be marshaled against the diagnosis of epithelioma. I have observed this type of lesion frequently enough to note that it has always presented the same appearance. Somewhere on the face, usually on the cheeks, of a girl or young woman of the age at which acne occurs and with evidence of past or present sebaceous disease, a lentil-sized or smaller lesion may be observed. The lesion is raised and plateau-like, indurated but not reddened or inflamed, and of a waxy appearance. At times the edges of the elevated flat surface present small shiny white pinpoint-sized papules, suggestive of milia. In my opinion the disease is a sebaceous one and is not malignant.

DR. DAVID L. SATENSTEIN This is the first case of its kind that I have seen. I have observed epitheliomas in young people but not lesions like this, and to make a snap diagnosis of epithelioma is rather courageous. If clinical impressions are being given, I think that a mole which is undergoing central atrophy and which is trying to clear itself is as good a guess as epithelioma. An epithelioma of that type being present for fifteen years without any history of breaking down cannot be called epithelioma of any kind, regardless of the age of the patient. A nevus undergoing atrophy by degeneration is sometimes observed. Some moles do undergo spontaneous involution, especially when associated with sebaceous glands.

DR. MAX SCHEER I do not think that the lesion is an epithelioma in the sense in which the term is used, that is, basal cell epithelioma. Against such a diagnosis is the small size of the lesion plus its fifteen years' duration. However, what it is I cannot suggest.

DR. LUDWIG OULMANN I am also of the opinion that the lesion is a basal cell epithelioma of the adnexa of the skin, on account of the pearly edges around the atrophic center.

I presented a case here last year in which there was a similar lesion on the chin. Dr. Satenstein made the biopsy and the diagnosis of basal cell epithelioma. The condition cleared up with high voltage roentgen ray therapy, although during the discussion at the meeting it was stated that in these cases roentgen radiation is usually without benefit.

DR. GEORGE C. ANDREWS I have been particularly interested in this condition. I have observed 3 other cases, and the conditions in all of them have been exactly the same clinically: small round lesions, with somewhat hard waxy shiny depressed centers surrounded by a wall of little papillary projections. I think the lesions always occur in young people, and they resemble nevi more than anything else. It seems to be a definite clinical entity.

Mycosis Fungoides with Pernicious Anemia? Presented by DR ANTHONY C CIPOLLARO

K G, a woman aged 60, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in September 1939, with a generalized eruption of eight months' duration. Prior to the onset of the present condition there had never been any cutaneous lesions.

The patches are irregular in size and shape. Some are definitely infiltrated, while others are lichenified. A few lesions show infiltrated concentric rings. The lesions on the ankles and on the lower third of both legs are eczematized and exudative. The skin and mucous membranes are pale and give the general appearance of anemia. The tongue is smooth and glossy, as in atrophic glossitis. The liver is palpable, but the spleen is not. The patient has had for some time numbness and tingling of the hands and feet.

Examination of the blood showed a color index of 1.1, which seems to support the diagnosis of pernicious anemia, and the following values: hemoglobin 80.4 per cent, erythrocytes 3,500,000 per cubic millimeter, polymorphonuclears 42 per cent, lymphocytes 46 per cent, eosinophils 5 per cent and monocytes 7 per cent.

The red cells showed slight anisocytosis. The Wassermann and Kahn reactions were negative.

DISCUSSION

DR FRED WISE: I do not think that the condition is mycosis fungoides, because there is no infiltration. The lesions are exudative and eczematous rather than dry and infiltrated. There is a slight degree of elevation and infiltration, peculiar to the advanced stage of mycosis fungoides. I think that the patient has pernicious anemia and probably eczema.

DR J FRANK FRASER: I agree with Dr Wise that the condition is not mycosis fungoides. The clinical picture does not support that diagnosis. Vitamin deficiency should be considered and also contact dermatitis from hair dye. The oozing dermatitis of the face and ears strongly suggests the latter.

DR ANTHONY C CIPOLLARO: When I examined the patient with Dr Lionel Rubin, our impression was that the lesions were infiltrated, and the diagnosis of mycosis fungoides suggested itself. Further examination of the blood showed a color index higher than 1. Because she also had glossitis and complained of numbness, we thought that the condition might be an unusual kind of mycosis fungoides and pernicious anemia. Therefore, we proceeded to institute studies to ascertain whether both diseases were present. We have ordered further blood studies, gastric analysis and also biopsy of specimens from two different areas.

NOTE—Histologic examination of tissue from one area showed eczema, and of a specimen from another area, mycosis fungoides. The question of pernicious anemia has not been settled, but the gastric analysis showed diminution of total acidity and no free hydrochloric acid.

A Case for Diagnosis (Livedo Racemosa?) Presented by DR ISADORE ROSEN.

F M, a woman aged 21, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Aug 21, 1939, with a generalized condition of seven years' duration.

The patient presents a decided bluish reticulated appearance over practically the entire body, particularly the extremities. When she was first seen six weeks ago there were several small ulcerations over the right foot, which have healed since.

Laboratory tests gave the following results

| | | |
|---|---------------------------------|---|
| Urinalysis | Sugar | None |
| | Albumin | None |
| Wassermann and Kahn reactions | | Negative |
| Histologic report | | Telangiectasia, possibly Ma
jocchi's purpura annularis
telangiectodes |
| Blood count | | |
| | Red blood cells | 3,800,000 per cubic millimeter |
| | White cells | 10,850 per cubic millimeter |
| | Hemoglobin (14.2 Gm per 100 cc) | 85.2 per cent |
| | Color index | 1.1 |
| Differential count (average of 200 cells) | | |
| | Polymorphonuclear neutrophils | 65 per cent |
| | Lymphocytes | 30 per cent |
| | Eosinophils | 1 per cent |
| | Basophils | 0 |
| | Monocytes | 4 per cent |

The patient had been examined at the medical clinic on Sept 18, 1938, with the following observations (1) overweight, (2) hypertrophied tonsils, (3) pain due to ovarian dysfunction and (4) dysmenorrhea

Roentgenograms of the feet and ankles taken at the New York Orthopedic Clinic on Aug 18, 1939 were normal

Histologic examination showed that the superficial blood vessels were dilated with edematous walls, and that there was considerable cellular infiltration and edema around them. The collagen bundles showed parenchymatous edema. The epidermis was essentially normal.

DISCUSSION

DR DAVID L. SATENSTEIN: On microscopic examination I observed more than was given in the report. The telangiectasis was not suggestive of degeneration but was the kind that usually goes on to degeneration. There were no hemorrhages or evidence of blood anywhere, there were no aneurysms. I could not make a diagnosis of purpura annularis telangiectodes, but I have observed the same kind of change in the blood vessels in cases in which I suggested the possibility of this disease.

DR LUDWIG OULMANN: The patient stated that the lesions become bluish red and more pronounced in the wintertime. A tuberculin test may be indicated. The question is whether this condition started with exposure to cold.

DR ISADORE ROSEN: The reason I presented this patient is not on account of the clinical diagnosis but because of the extensive involvement. I have never observed a patient with this condition in whom so large an area was involved. I am at a loss as to how to treat her, owing to the persistence of the clinical features which have remained unchanged for seven years.

Xanthoma Tuberosum Multiplex Presented by DR ANTHONY C. CIPOLLARO.

K. L., a housewife aged 43, born in America, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has had this condition for fifteen years. The patient stated that about fifteen years ago she began having lesions on the extensor surfaces of both elbows. Later, lesions developed on the hands, knees and toes. During the past fifteen years the lesions have become progressively worse. About eleven years ago she received injections of insulin and about five years ago some of the lesions were removed surgically. In some of the sites from which lesions were removed new lesions developed.

The patient now presents on the extensor aspects of the elbows nodular lesions varying in size from that of a marble to that of an English walnut. The lesions are raised, hard and canary yellow. There is no tenderness, and there is no attachment to the underlying structures. They are freely movable. On the extensor surfaces of the knees are lesions which are similar except that they are smaller. On the palmar and dorsal surfaces of most of the fingers of both hands the lesions are similar to those on the elbows. Those which are on the toes are of the same character but smaller than those on the hands. The rest of the body, including the eyelids, is free of lesions.

The cholesterol content of the blood was determined and found to be within normal limits.

DISCUSSION

DR ISADORE ROSEN This case is unusual on account of the extensive involvement and the fibrosis of the xanthomatous lesions. Undoubtedly there is a disturbance of the physiology of the liver and pancreas, these being the organs that control fat metabolism. I have observed temporary improvement in some of these conditions from a diet with restricted intake of fat and from ingestion of calcium.

DR FRED WISE I have had no success with a fat-free diet in patients with xanthoma tuberosum, although I did not give calcium internally.

DR ANTHONY C CIPOLLARO I shall follow Dr Rosen's suggestions and give her a fat-free diet and solution of calcium hydroxide.

Lupus Erythematosus Presented by DR MAURICE J COSTELLO

S S, a man aged 54, was presented before this society in February 1938 by Dr Bloom (*ARCH DERMAT & SYPH* 38 114 [July] 1938).

DISCUSSION

DR ANTHONY C CIPOLLARO My impression is that the patient has one disease, and that that disease is lupus erythematosus.

DR MAX SCHEER My impression is that the patient probably has sarcoid. Particularly the lesion on the abdomen is a definite infiltrated lichenoid sarcoid lesion. However, the lesions on the back have no infiltration and by themselves look like lupus erythematosus. It is possible that the patient has two diseases, lupus erythematosus and sarcoid.

DR DAVID BLOOM I observed this patient for many years. When I first saw him he had an erythematous thickened plaque on his forehead which was diagnosed as sarcoid. The diagnosis was not confirmed by the histologic report. The response of the lesion to roentgen therapy suggested the correctness of the diagnosis of sarcoid, in contradistinction to lupus erythematosus, which does not respond to this agent. The lesion on the left upper eyelid, however, suggested lupus erythematosus but has not responded to gold therapy. The lesions on the trunk which the patient presents tonight and which I now see for the first time do not suggest lupus erythematosus.

DR PAUL E BECHET I believe that the lesions strongly suggest lupus erythematosus of the bullous type. The scales are apparently extremely loose and moist, with evidence of bullae here and there.

DR MAURICE J COSTELLO The patient was presented because of the resemblance of some of the lesions to sarcoid, especially those on the back, and because of the favorable response of those lesions to fractional doses of roentgen rays.

Kaposi's Sarcoma and Leukonychia Presented by DR MAURICE J COSTELLO

O G, a man aged 40, was born in Austria and has lived in this country since he was 5 years old. Three brothers are living and well. His parents died of natural causes, and no other member of his family has a condition similar to his.

The eruption which he now presents began in 1932 and was accompanied by swelling of the left lower extremity. Soon pigmented pea-sized to dime-sized nodules appeared on the upper and lower extremities, and a tentative diagnosis of Kaposi's sarcoma was made, which was confirmed by histologic examination. His left wrist was fractured in 1923, and when the eruption appeared, the left but not the right forearm was involved. He also has leukonychia involving the distal two thirds of the finger nails and toe nails. There are no lesions on the mucous membrane. His Wassermann reaction was negative.

Small doses of roentgen rays and radium have been applied, with complete disappearance of the lesions treated.

Tattoo Marks Result of Attempts to Remove Them Presented by DR PAUL E BECHET

J P, a man aged 26, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital today. On both forearms are large and elaborate tattoo marks, which were applied nine years ago. Several applications of nitric acid have been made to the tattoo on the left arm, causing a flat scar on one section and a rather unsightly hypertrophic scar on another. Both scars measure about 2 or 3 cm in diameter. On the right arm electrodesiccation over a small area has given excellent results. The case is presented in order to elicit suggestions as to therapy.

DISCUSSION

DR DAVID BROOM: My experience with a few cases in which I removed tattoo marks by electrodesiccation leads me to believe that electrodesiccation is simpler and perhaps better than the tannic acid method. Following electrodesiccation and removal of the skin overlying the pigment, removal of most of the pigment with a curet is necessary. The area is again desiccated after curettage. A smooth scar is the result, which is preferred by these patients to any tattoo which they want to have removed.

DR LUDWIG OULMANN: Besides other methods, I applied the same method Dr Bloom described, with good results. Some of the pigment cannot be removed with the first application but will be removed by a second treatment.

DR PAUL E BECHET: The tattoo marks on this particular patient are extremely large, and in my opinion the areas, no matter how they might be treated, will invariably present severe scars. I should advise the patient not to have them removed.

MINNESOTA DERMATOLOGICAL SOCIETY

E M RUSTEN, M D, *President*

F W LYNCH, M D, *Secretary*

St Paul, Oct 20, 1939

Lichen Planus Hypertrophicus of the Legs, with Lupus Erythematosus of the Face. Presented by DR J F MADDEN, St Paul

Mrs H A, aged 48, first showed an eruption on the anterior surfaces of the legs in 1937, which appeared as flat, dark red to brown, itchy papules. They gradually enlarged until they are now elevated verrucous reddish brown nodules varying in size from that of a marble to that of a large walnut.

In July 1939 the patient noticed small, scaly, slightly elevated, erythematous macules on the cheeks and on the bridge of the nose. They have increased in

size and have become confluent. The lesions appear as irregular erythematous maculopapules with a tightly adherent scale. Some of the lesions have central atrophy and scarring.

The Wassermann reaction of the blood was negative. A Mantoux test gave a negative result. Roentgenograms of the chest were normal.

Histologic sections are shown.

Zosteriform Lichen Planus Presented by DR J F MADDEN, St Paul

W M, a boy aged 13, first noticed in April 1939 an eruption of bright red papules on the right side of the abdomen. The lesions gradually spread posteriorly to the midline. The eruption now extends from the tenth dorsal to the first lumbar vertebra around the right flank to the midline. The only change the patient has noticed is slight fading in the color. The eruption is made up of closely packed angular violaceous flat-topped or delled papules the size of a pin-head. There is mild itching. The eruption is also present in the mouth where it involves almost the entire surface of the buccal mucous membrane.

The Wassermann reaction of the blood was negative.

Lichen Planus Hypertrophicus Presented by DR J F MADDEN, St Paul

S R, a Negro aged 60, first noticed an eruption on the anterior surfaces of the lower extremities in 1934. The lesions were itchy and soon developed into elevated verrucous papules. The lesions now cover the anterior surfaces of both legs. They are dully erythematous, and some are excoriated. The papules vary in size from that of a pea to that of a dime.

The Wassermann reaction of the blood was negative.

DISCUSSION

DR H E MICHELSON, Minneapolis. Combinations of cutaneous diseases in a patient are extremely interesting. I think lichen planus occurring with psoriasis is the most common combination, and lupus erythematosus with lichen-planus-like lesions is also often observed. There seem to be phases in the development of psoriasis in which it is almost impossible to tell whether the patient is going to have lichen planus or psoriasis.

DR WILLIAM HILL, Providence, R I (by invitation). The histologic section presented is not characteristic of lichen planus. There are hyperkeratosis, increase in the granular layer and acanthosis. The usual infiltrate is not thrown up against the basal layer in this section but is mostly perivascular. If the condition is lichen planus, it is atypical histologically.

DR LOUIS A BRUNSTING, Rochester. There were lesions of lichen planus in the mouth and a few scattered over the trunk, but primarily they were localized to a segmental band of skin on the left side of the back and on the left side. Perhaps there has been some mild involvement with herpes zoster, and the lesions of lichen planus have developed at this site as a result of irritation in the form of a modified Kobner's phenomenon. This type of zosteriform distribution is occasionally seen in lymphoblastoma.

DR STEPHAN EPSTEIN, Marshfield, Wis (associate member). Dr Brunsting discussed the relation of lichen planus and the nervous system. I wonder whether any one has had experience with vitamin B treatment of lichen planus. I hesitate to report the following observations on account of the small number of cases. One of my patients received vitamin B complex (betalin compound, Lilly) on account of an arsenical zoster, the lichen planus, which had been rather resistant, cleared up rapidly afterward. Since then I have treated 2 more patients, 1 received

the vitamin B complex (betalin compound, Lilly) and now is well. The other has been treated with pure thiamin chloride (vitamin B₁) for six weeks and is improving considerably.

NOTE—The second patient continued to improve and three months after the meeting was almost well.

DR CARL W LAYMON, Minneapolis. The treatment of lichen planus is difficult. In some cases any of the recognized therapeutic measures produces favorable results, while in other instances the disease proves resistant to everything which is attempted, thus making it difficult to appraise the value of any one kind of treatment. I believe that judgment concerning vitamin B therapy should be reserved until there has been time to study it more.

Depigmentation at the Site of Chronic Contact Eczema. Presented by
DR J F MADDEN, St Paul

S M, a Negro aged 53, stated that an eruption appeared in the summer of 1936. It disappeared and recurred in February 1939. There is a weeping eczematoid eruption on the face, neck, arms, genitalia and legs. The skin of the cubital and popliteal spaces, genitalia, face and neck is lichenified. There is depigmentation at the sites of the eruption which is especially pronounced in the lichenified portions.

The Wassermann reaction of the blood was negative. Examination of the blood showed 66 per cent hemoglobin, 3,560,000 erythrocytes per cubic millimeter and 13,200 leukocytes per cubic millimeter, with 62 per cent polymorphonuclears, 34 per cent lymphocytes and 2 per cent monocytes. The result of urinalysis was normal.

DISCUSSION

DR F W LYNCH, St Paul. The depigmentation in this case brings to mind the group of cases recently reported by Oliver, Schwartz and Warren (*J. A. M. A.* 113:927 [Sept 2] 1939) in which vitiligo resulted from some ingredient in rubber gloves. The Negro presented by Drs Oliver, Schwartz and Warren, at the recent meeting of the Dermatological Conference of the Mississippi Valley (this issue, page 587) showed little evidence of dermatitis, suggesting that the loss of pigment may have been a more specific action than that in the case presented tonight in which the dermatitis was severe.

Syphilis (Treated); Lymphogranuloma Venereum? Presented by DR J F
MADDEN, St. Paul

C Z, a man aged 32, noted a chancre developing on the shaft of the penis in November 1931 and received immediate treatment. He was treated almost continuously until 1936. The Wassermann reaction of the blood has always been 4 plus. The patient was regular in his treatments. In the summer of 1937 a sore throat developed accompanying a cold. The sore throat persisted, and he noticed small white blisters appearing on the left side of the pharynx. The lesions in the throat disappeared in about a month and recurred in January 1938. When the patient was seen in January there was an ulcer on the left side of the pharynx. When he was seen in April 1939 the ulcer had extended into the nasopharynx and the nose. The ulcer is superficial, discharges pus and has a ragged border. The patient's head feels congested, and it is difficult for him to breathe through the nose. The ulcer has not changed appreciably since I first observed it in April 1939. The patient has retained his weight and seems in good general health. He has had continuous heavy antisyphilitic treatment with arsenic and bismuth, and with malarial therapy, which consisted of eight good malarial paroxysms during the past year and a half. He was given sulfanilamide during the past two weeks but could not tolerate enough of the drug so that a blood concentration of over

5.5 mg per hundred cubic centimeters could be established. The patient's treatment since 1931 is shown in the accompanying tabulation.

The Wassermann reaction of the blood was repeatedly 4 plus. Repeated Frei tests with mouse brain antigen gave positive results. Control tests on other patients gave negative results. Examination of the blood showed 78 per cent hemoglobin and 13,300 leukocytes per cubic millimeter, with 80 per cent neutrophils, 17 per cent lymphocytes, 2 per cent monocytes and 1 per cent basophils. The spinal fluid was normal when examined April 19, 1939. Roentgenograms of the mandibular and maxillary sinuses showed cloudiness in the right and left antrums. There was a dense body in the right frontal sinus which was thought to be an osteoma. Roentgenograms of the chest were normal. A Mantoux test gave a negative result.

Histologic sections are shown.

| Year | Bismuth Subsalicylate in Oil | | Neoarsphenamine | | Silver Arsphenamine | | Mapharsen | | Mercuric Succinimide | |
|-------|------------------------------|------------|------------------|------------|---------------------|------------|------------------|------------|----------------------|------------|
| | No of Injections | Amount, Gm | No of Injections | Amount, Gm | No of Injections | Amount, Gm | No of Injections | Amount, Gm | No of Injections | Amount, Gm |
| 1931 | 1 | 0.13 | 6 | 0.6 | | | | | | |
| 1932 | 10 | 0.13 | 15 | 0.6 | | | | | | |
| 1933 | 6 | 0.13 | 9 | 0.6 | | | | | | |
| 1934 | 7 | 0.13 | | | | | | | | |
| 1935 | 4 | 0.13 | 5 | 0.6 | | | | | | |
| 1936 | | | | | | | | | | |
| 1937 | 4 | 0.13 | 20 | 0.6 | | | | | | |
| | 4 | 0.26 | | | | | | | | |
| 1938 | 5 | 0.13 | 29 | 0.6 | | | | | | |
| 1939 | 5 | 0.13 | 14 | 0.6 | 1 | 1 | 4 | 0.06 | 20 | 0.01 |
| | | | | | 1 | 2 | | | | |
| | | | | | 7 | 3 | | | | |
| Total | 46 | | 95 | | 9 | | 4 | | 20 | |

DISCUSSION

DR J F MADDEN, St Paul. I do not think that the ulcer is self induced, because the patient has been under constant observation for a period of several weeks with no change in the lesion. I do not think that it is a syphilitic ulcer because of the complete lack of response to treatment for syphilis and the clinical and histologic observations.

DR H E MICHELSON, Minneapolis. I can make no positive statements about the patient, but I feel definitely that he does not have syphilis. If the patient had malignant syphilis he would be much sicker than he is, and undoubtedly the ulceration would have proceeded through the palate. I have no diagnosis to offer.

DR L A BRUNSTING, Rochester. If tuberculosis and malignancy can be excluded definitely, I favor the possibility of syphilis, because of the youth of the patient, his general well-being and the persistence of the strongly positive Wassermann and flocculation reactions of the blood. Dermatitis artefacta is an outside possibility. In spite of the intensive regimen of antisyphilitic treatment that has been carried out, I suggest a change of treatment: old arsphenamine, mercury instead of bismuth, iodides and periodic injections of typhoid vaccine. Not much consideration need be given to the diagnosis of lymphogranuloma venereum.

Xanthoma Presented by DR J F MADDEN, St Paul

J S, a man aged 55, has pulmonary tuberculosis with cavitation. He first noticed a pea-sized bluish elevated papule on the lateral surface of the middle third of the left leg about 1932. This has gradually increased until it is now the size of a quarter. The nodule is slightly depressed, reddish purple and asymptomatic. The Wassermann reaction of the blood was negative.

DISCUSSION

DR WILLIAM HILL, Rochester (by invitation) In looking at the biopsy specimen I was impressed with the abnormal amount of fibrosis. Foam cells, giant cells of the Touton type and some pigmentation were also seen. The picture is undoubtedly one of xanthoma. However, all these features can be observed in histiocytoma, the possibility of which should be considered.

DR CARL W. LAYMON, Minneapolis In my opinion both the clinical appearance of the lesion and the appearance of the histologic sections favor a diagnosis of xanthoma. Studies of the blood lipoids should be made. Although the lesion clinically and superficially resembles those of necrobiosis, the sections seem to be inconsistent with such a diagnosis.

DR LOUIS A. BRUNSTING, Rochester A suggestion that was brought out at another meeting recently is the subcutaneous injection of a dilute (1 per cent) solution of saccharated ferric oxide in the vicinity of the lesions. When the tissue is excised one or two days later, the prussian blue reaction in the large cells which resemble histiocytes will give some idea of the degree of phagocytosis that is present.

DR H. E. MICHELSON, Minneapolis I think that the patient has xanthoma, but what type of xanthoma it is hard for me to say. As far as the discussion on histiocytes is concerned, some of the members of the society will remember that Oscar Gans said, "When we know all about histiocytes, we will know a great deal about the physiology and pathology of skin."

**A Case for Diagnosis (Lymphoblastoma [Hodgkin's Disease of the Skin?]
Benign Lymphadenoid Granuloma [Lymphocytoma]?). Presented by
DR J. F. MADDEN, St. Paul**

Miss E. L., aged 25, stated that painless round elevated papules appeared on the shoulders during the early part of 1936. Since then the lesions have grown slowly but steadily. They are itchy and at times scaly. The color varies from deep purple to dark brown. They vary in size from that of a pea to one nodule as large as a 50 cent piece. The lesions are of a firm rubbery consistency and are slightly raised above the surrounding surface of the skin.

The patient had had no treatment before I saw her on March 30, 1939. She stated that she did not take any medication regularly. She was given anacin (a mixture of acetophenetidin, acetylsalicylic acid, quinine sulfate and caffeine), acetylsalicylic acid and phenolphthalein, with no change in the lesions. A general physical examination revealed no abnormality. There was no generalized lymphadenopathy. Her temperature was taken at 8 a. m., 4 p. m. and 8 p. m. for two weeks and was normal at all times. The larger lesions were treated with approximately 800 r of unfiltered roentgen rays between May 10 and August 9. The lesions showed a temporary regression after each treatment.

The Wassermann reaction of the blood was negative. The urinalysis was normal. The results of examination of the blood at various times are shown in the accompanying tabulation.

| Date | Hemo-
globin,
per Cent | Red
Blood Cells
per C. Mm | White
Blood Cells
per C. Mm | Lympho-
cytes,
per Cent | Poly-
morpho-
nuclears,
per Cent | Neutro-
phils,
per Cent | Eosino-
phils,
per Cent | Baso-
phils,
per Cent |
|------------|------------------------------|---------------------------------|-----------------------------------|-------------------------------|---|-------------------------------|-------------------------------|-----------------------------|
| May 10 | 76 | 3,810,000 | 9,950 | 56 | 44 | | | |
| May 24 | | | 6,450 | 60 | 37 | | 2 | 2 |
| May 31 | | | 5,000 | 80 | 20 | | | |
| June 21 | | | 6,000 | 71 | 27 | | 1 | 1 |
| August 16 | | | 8,550 | 48 | | 50 | 2 | |
| October 11 | 74 | | 6,800 | 30 | 65 | | | |

Histologic sections are shown. All biopsy specimens were taken from untreated lesions.

DISCUSSION

DR CARL W LAYMON, Minneapolis The location and the type of lesion in this case are against a diagnosis of lymphocytoma, in which the lesions are usually papules or nodules occurring on the face and sometimes on the genitals or other areas The course is prolonged, although some conditions respond to treatment with arsenic and irradiation The histologic picture of lymphocytoma resembles that of an ordinary lymph node

DR STEPHAN EPSTEIN, Marshfield, Wis (associate member) The clinical picture as presented by this case is different from that described as lymphocytoma, the literature on which I reviewed in 1935 (*Arch f Dermat u Syph* 173 181, 1935) The microscopic picture in this case is different too and does not show the lymph follicles with germinal centers which are so typical of lymphocytoma but practically never occur in leukemic conditions The relation of lymphocytoma to lymphoblastoma is still a matter of discussion, but so far in none of the cases of true lymphocytoma has the condition turned into leukemia, although the patients of Jadassohn and Biberstein have been under observation for a period of ten years

DR J F MADDEN, St Paul All the biopsy specimens were taken from untreated lesions The first histologic section showed a massive lymphocytic infiltrate, while the later sections showed a diminution of lymphocytic infiltrate and an increased fibrosis No Sternberg cells were observed in the sections

Scrofuloderma Pulmonary Tuberculosis Presented by DR J F MADDEN, St Paul

Mrs L O, aged 31, in January 1934 was treated for subacute left salpingitis The pain disappeared, but the patient lost weight and hemoptysis developed A diagnosis of pulmonary tuberculosis with cavitation was made, and the patient was hospitalized but was discharged in 1936 with an inactive condition She was fairly comfortable until April 1938, when she returned to the hospital because of a pain in the left lower part of the abdomen A painful mass the size of an apple was found to the left of the uterus In about a week a painful bluish discolored area developed in the left inguinal region The site soon ruptured, and there has been an extensive discharging sinus to the present time

The Wassermann reaction of the blood was negative The Frei test gave a negative result Cultures and smears from the pus showed no tubercle bacilli

DISCUSSION

DR H E MICHELSON, Minneapolis Scrofuloderma is, of course, most common over gland-bearing regions, but scrofuloderma in the inguinal region is rare and when it does occur often has its source from deeper involvements, such as tuberculous salpingitis or even peritonitis The late J B Murphy wrote a classic description of an inguinal sinus originating in a tuberculous appendix In the patient presented the scrofuloderma has its origin in the tuberculous salpinx

Lupus Vulgaris; Ulcers of the Tongue (Unknown Cause), Osteomyelitis of the Right Humerus Presented by DR J F MADDEN, St Paul

Mr F H, a man aged 50, was surgically treated in 1920 for cervical adenitis on the left side which broke down and formed numerous draining sinuses The entire tracts and glands were excised After this an eruption developed at the site of the scar

In 1937 ulcers developed on the tip and lateral margins of the tongue The ulcers were from pea-sized to bean-sized, superficial and painful During 1939 the ulcers were treated with an 85 per cent solution of lactic acid and have almost healed

During the latter part of 1937 the patient thought that he pulled a muscle while at work A severe pain developed in the right shoulder There is still a draining sinus from the chronic osteomyelitis at the head of the humerus

Roentgenograms of the humerus showed chronic osteomyelitis Repeated roentgenograms of the chest showed no evidence of pulmonary tuberculosis Repeated

examinations of the sputum, examinations of the pus from the sinus leading from the humerus and smears from the ulcers on the tongue failed to reveal tubercle bacilli. Guinea pig inoculations gave negative reactions. The Wassermann reaction of the blood was repeatedly negative. A Mantoux test gave a strongly positive result.

Histologic sections are shown.

DISCUSSION

DR. J. F. MADDEN, St. Paul. It is my impression that the ulcers on the tongue are those of superficial lupus vulgaris. This opinion could not be substantiated because a biopsy of an ulcer was not permitted.

DR. STEPHAN EPSTEIN, Marshfield, Wis. (associate member). The patient presents a superficial type of lupus vulgaris with a color more yellowish than usual. According to the history the sequence may have been a tuberculous glandular infection and then scrofuloderma which turned into lupus vulgaris. There seemed to be some red nodules around the healed ulcer of the tongue, which might have been a tuberculous ulcer. The osteomyelitis might have been tuberculous too. The patient recalls a patient of mine who suffered from a tuberculous osteomyelitis and showed the same type of superficial lupus vulgaris without active involvement of the lungs; he finally died of a tuberculous meningitis.

DR. H. E. MICHELSON, Minneapolis. I am glad that this patient has been presented tonight, because the case brings to attention the fact that lupus vulgaris is a disease which has many and varied manifestations. A large percentage of patients with lupus have involvement of the mucous membrane, especially in the nose and mouth, and the condition in the patient presented is one type of tuberculosis of the mucosae which heals with proper treatment.

Calcinosis Cutis Presented by DR. J. F. MADDEN, St. Paul

Mrs. J. J., aged 55, noticed pea-sized hard papules in the subcutaneous tissue of the right arm in 1919. They have gradually enlarged until they are now the size of marbles. Some of the lesions have become confluent to form elongated plaques. The skin is erythematous and glistening over some of the lesions, while it appears to be normal over others. The skin seems to be attached to the lesions. There is one nodule on the left thigh. The patient had hypodermic injections in the arm in 1910 when she had pneumonia but had none during the nine years before the lesions appeared.

The Wassermann reaction of the blood was negative. The calcium content of the blood was 10 mg. per hundred cubic centimeters.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester. It seems safe to conclude that the lesions are delayed reactions at the site of injections of foreign material. In the absence of a general disturbance of metabolism, surgical excision could be carried out, at least at one site, as a trial.

PHILADELPHIA DERMATOLOGICAL SOCIETY

JOSEPH V. KLAUDER, M.D., *Chairman*

HERMAN BEERMAN, M.D., *Secretary*

Oct. 20, 1939

Vitiligo with Superimposed Pellagra. Presented by DR. DOUGLASS A. DECKER, Allentown, Pa.

J. M., a white man aged 44, presents typical vitiligo on the face, ears, arms and chest. On the face, ears, chest and dorsa of the hands and fingers there is a

symmetric erythema associated with atrophy and irregular areas of hyperpigmentation. The condition has been present for four years, always occurring in the summer and disappearing in the winter. All but the vitiligo disappeared while the patient was treated in the hospital with a high vitamin diet. Five blood counts were normal. The Wassermann reaction of the blood was negative. A roentgenogram of the bony thorax and of the lungs was normal. Histologic examination showed mucinoid degeneration of the corium accompanied by erosion of the epidermis. There was no histologic evidence of lupus erythematosus.

DISCUSSION

DR FRANK C KNOWLES. I believe that the condition in this case is lupus erythematosus. I do not think that it resembles pellagra on the hands, it is not the proper color. I think that the pigmentation on the face is subsequent to lesions of lupus erythematosus.

DR J V KLAUDER. I agree with Dr Knowles. Pellagra does not involve the dorsal surface of the terminal phalanx of the finger. It usually extends to the second to the last phalanx.

DR FRED D WEIDMAN. When the patient was first seen, the diagnoses considered were lupus erythematosus and leukoderma. Since that time I have elicited a history of general constitutional symptoms which agree with those of pellagra, and recently I noticed lesions in the distribution known as Casal's necklace. The depigmentation was interesting in the light of the preexisting hyperpigmentation, and I can understand how the disease, pellagra or lupus erythematosus or whatever it is, may have had an effect on the adrenals or other pigment-stimulating or supportive mechanism which at first caused hyperpigmentation, and then by continuation of that the function was run to the point of exhaustion, whereupon there succeeded the depigmentation.

DR DOUGLASS A DECKER, Allentown, Pa. I saw the man for the first time during the summer, when he had to be led into the clinic by his wife. He was definitely demented. His skin cleared up in two weeks after he was hospitalized and treated with a high caloric and high vitamin diet. He had the typical signs of pellagra—erythema, bullae and vesicles on the backs of the hands and on the face and sternum, and his response to the high vitamin therapy seemed to me to be evidence that he had pellagra. His blood count was normal, and I observed no signs of lupus. He was not placed in bed but was given the high vitamin diet and allowed to wander around the ward. I was informed that his diet at home had contained no vitamins. He drank a little wine but was not an alcoholic addict. Since his discharge from the hospital the inflammatory reaction has recurred on the old sites. He has not yet been given vitamins again.

DR EDWARD F CORSON. Some patients with lupus erythematosus also do well on a high vitamin diet. I have had considerable success with a few patients in whom the condition was chronic who were treated especially with vitamin B₁. I think that the condition in this case is an example of a vitiliginous type of lupus erythematosus. I do not think that the tongue is at all typical of pellagra.

Lichen Nitidus Presented by DR DOUGLASS A DECKER, Allentown, Pa.

On the backs of the hands, wrists, arms, shaft of the penis, back and thighs of A L., a Negro aged 19, are patches of discrete pinhead-sized dull white papules. In the same areas on the arms the hair follicles are involved. The condition has been present for eight months. The results of the medical examination and the Wassermann reaction of the blood were negative. Permission for biopsy was refused by the patient. He has been treated with protiodide of mercury without improvement.

DISCUSSION

DR FRED D WEIDMAN. I was not so sure when I saw this patient last week that he had lichen nitidus, because close examination in a good light showed that

some of the papules are thickly spattered indeed and are present in other places than the wrists, the eruption is spread widely on the back, for example. A large proportion of the papules are located around the hair follicles, a larger proportion than one would expect from the law of averages. I was hoping that other diagnoses would be given for this case. I could not make the diagnosis of pityriasis rubra pilaris, the condition is not rubra. It is conspicuously not pilaris. I was not satisfied with the diagnosis of lichen nitidus.

DR EDWARD F. CORSON: I think the condition is lichen nitidus. It does not seem inflammatory.

DR FRED D. WEIDMAN: If this is lichen nitidus, there seems to be some implication of the hair follicle apparatus, which may be of some importance in the pathogenesis of the lesions.

A Case for Diagnosis (Lichen Planus? Dermatitis Medicamentosa from Bismuth?). Presented by DR H. E. TWINING

B. R., a Negress aged 45, presents sharply defined dry and slightly scaly maculopapular lesions scattered symmetrically on the entire body. Some of the lesions have a waxy, shiny appearance, but for the most part they are inky black. There are linear lesions on the oral mucous membranes. In March 1939 the patient began to receive antisyphilitic treatment, and shortly thereafter there occurred a severely pruritic macular eruption of widespread distribution. The Wassermann and Kahn reactions of the blood were positive. Lichen planus was considered clinically, but the diagnosis was doubted in view of the history of injections of a bismuth preparation. The same problems arise in the histologic studies, but in the opinion of Dr. Weidman the points which favored bismuth eruption were (a) the pronounced leukocytic features and (b) the extension around the hair follicles, the lymphocytic features were not pronounced. He stated, too, that the dyskeratosis was against a diagnosis of lichen planus, moreover, the edema around the basement membrane was certainly not outspoken. Assuming that this was a bismuth dermatitis, the similarity of the processes to those of lichen planus would be suggestive as to the cause of lichen planus, namely, a toxic agent.

DISCUSSION

DR CARROLL S. WRIGHT: Every one who has examined the mouth of the patient tonight could see the involvement of the buccal mucosa and the eruption on the tongue, typical of lichen planus. It is sometimes difficult to make a diagnosis from the cutaneous lesions of a Negro. If the patient has lichen planus, she has three types of lesions, namely, annular, atrophic and hypertrophic, and apparently they are the result of antisyphilitic therapy, according to her history.

DR DONALD M. PILLSBURY: I think that there is another interesting point in this case in reference to the lesions of the scalp. On the sides of the scalp she has hypertrophic and hyperpigmented lesions with central atrophy. On the vertex are lesions which are indistinguishable, to my mind, from those of pseudopelade. If the condition is lichen planus, it is one of the best demonstrations of the oneness of pseudopelade and lichen planus that has ever been presented.

DR FRANK C. KNOWLES: I do not understand how one can make a diagnosis of lichen planus in the present case. The lesions on the face are almost nodular, and as Dr. Pillsbury has brought out, there are lesions on the scalp, contrary to all conceptions of the disease. I hesitate to make a diagnosis, but I think there are two conditions to suggest in the present circumstances. One would be tuberculosis of the skin and the other pemphigus vegetans.

DR FRED D. WEIDMAN: One thing that strikes me is the inky blackness of the lesions. I am accustomed to seeing hyperpigmentation in Negroes, and only occasionally have I seen inky black lesions. Reports have been published of

bismuth pigmentations in which the nuciospectroscopic method had shown that there was more than one metal concerned in the pigmentation of the skin and that perhaps there was a synergistic effect, a deposit of one metal, say silver, together with the deposit of another metal. I wonder whether some of this inky black is referable to bismuth which has been laid down in addition to a melanosis. When I first saw the patient I thought of Schaumann's disease. She does have a pronounced generalized lymphadenopathy. Some of the lesions on the face show definite nodules in the periphery. It is true that I reported histologic observations in favor of lichen planus, but I do not know whether a nodule was selected for biopsy. I think that an additional biopsy, of one of the nodular lesions, should be performed, and if possible also a biopsy of one of the enlarged lymph nodes. The whole gamut of examinations for Schaumann's disease or the anergic type of tuberculosis in the American Negro should be run. I am not satisfied that this is a clearcut case of lichen planus, additional examinations should be made.

DR CARROLL S. WRIGHT: It seems to me that Dr. Weidman did not see the same thing in the mouth as I did. There were definite white radiating lines on the buccal mucosa which stood out more than the pigmentation. I do not see any other possible diagnosis for the lesions of the mucous membrane than lichen planus.

DR H. E. TWINING: I am inclined to think that the condition is lichen planus. The woman stated that when intravenous therapy, possibly with neoarsphenamine, was employed, she became considerably worse both objectively and subjectively and that as soon as the therapy was stopped she began to improve.

DR SIGMUND S. GREENBAUM: I should like to ask Dr. Pillsbury whether he is considering pseudopelade the same condition as the Graham Little type of lesions of the scalp occurring in lichen planus.

DR DONALD M. PILLSBURY: I think Graham Little intimated that the two conditions are the same.

DR SIGMUND S. GREENBAUM: The oral lesions in this patient are typical of lichen planus. A case of lichen planus due to gold sodium thiosulfate was presented at the last Atlantic Dermatologic Conference, in Baltimore, and a case of lichen planus after the administration of arsphenamine and bismuth was presented before this society last year (*ARCH. DERMAT. & SYPH.* 37:690 [April] 1938). Brocq was the first, I think, to consider lichen planus a cutaneous reaction to a variety of agents, some of which are known and some of which are unknown, such as bismuth occasionally and sometimes arsphenamine. The patient is a Negress, and it is possible that the hypertrophic lesions are keloidal.

DR FRANK C. KNOWLES: Where some of the lesions have gone away there will be permanent depigmented areas. There is a distinct tendency to scar formation. I think that would almost prove the fact that the condition could not be lichen planus.

DR SIGMUND S. GREENBAUM: I thought that the section under the microscope was typically lichen planus, and some of the lesions on the skin are typically annular lichen planus, some of them having undergone pigmentary atrophy, with others showing superficial epidermal atrophy.

DR FRED D. WEIDMAN: I squeezed one of the lesions on the back of the finger, and there was oozing of fluid, which is not typical of lichen planus.

DR J. V. KLAUDER: When I examined this woman several weeks ago, I did not see any nodules. The lesions on the chest are recent. It is likely that the picture has changed.

Darier's Disease in a Woman Presented by DR. THOMAS BUTTERWORTH, Reading, Pa.

E. B., a white woman aged 25, has an eruption of small brownish warty and papular lesions on the forearms, face, neck, shoulders and upper anterior portion

of her trunk. The intervening skin is now approaching normal, but a few weeks ago there was slight erythema between the lesions (sunburn?). She also has only scaling of the scalp, which has improved under therapy. There are numerous warty excrescences on the palms and soles and white longitudinal bands and striations on some of the nails. There are small red papules on the dorsum of the tongue. The condition has been present for four years. The patient's mother has a cutaneous disease, but of a different type. Urinalysis gave negative results, and the Wassermann reaction of the blood was negative. The sugar content of the blood was 100 mg per hundred cubic centimeters, the urea nitrogen content, 9 mg, and the protein nitrogen, 33.3 mg. A blood count was essentially normal. The morphologic appearance of the erythrocytes was normal. Histologic examination showed localized hyperkeratosis with variable parakeratosis. "Bird eyes" or "corps ronds," the so-called grains and intrapapillary cysts gave a picture compatible with Darier's disease. Various local applications have been without effect on the papular elements.

DISCUSSION

DR J. M. SCHILDKRAUT, Trenton, N. J. I think that this case of Darier's disease in a woman is the first that has been presented before this society.

DR HERMAN BEERMAN. Two weeks ago I saw a woman with Darier's disease at the Hospital of the University of Pennsylvania.

Epithelioma of the Penis Presented by DR THOMAS BUTTERWORTH, Reading, Pa.

T. P. M., a white man aged 62, presents an ulcer 20 mm in diameter, with an irregular firm border, on the dorsal surface of the prepuce. The lesion is friable and bleeds freely on slight trauma. The inguinal lymph nodes are palpable, particularly on the left side. The condition began three years ago as a scratch on the prepuce, which healed for several weeks. It then ulcerated and gradually spread to its present size. The Kahn and Kolmer reactions were negative. Histologic examination showed a superficially ulcerated squamous cell epithelioma with scarcely a vestige of keratinization (grade 4 of Broder's index).

DISCUSSION

DR FRANK C. KNOWLES. Did the lesion arise on an area of erythroplasia, or is there a history of trauma?

DR THOMAS BUTTERWORTH, Reading, Pa. The patient described it as a small scratch, not erythroplasia.

DR J. M. SCHILDKRAUT, Trenton, N. J. I saw a patient in whom a similar lesion was treated by electrocoagulation, and a few years later there was extreme induration in the groins. The process finally killed the patient, whereas if he had been treated by amputation and removal of the inguinal lymph nodes the chance of recovery might have been excellent.

Balanitis Xerotica Obliterans Presented by DR THOMAS BUTTERWORTH, Reading, Pa.

W. A. K., a white man aged 52, presents slightly depressed firm, glazed whitened spots on the skin of the glans penis in irregular patches for about 1 to 1.5 cm about the urinary meatus. The patient says that he has not had gonorrhea but that he had a chancre on the prepuce twenty-five years ago, with no generalized rash. He has had forty intragluteal injections and one intravenous injection. The right testis was removed five years ago for a discharging condition of unknown nature. He has noticed whitening of the skin of the glans for about six or seven years. For the past two years he has noticed that the urinary stream

was becoming smaller. There has been occasional minor itching of the foreskin. Meatotomy was performed five days ago. The Wassermann reaction of the blood was strongly positive.

DISCUSSION

DR FRED D WEIDMAN. In xerosis ordinarily I think of an epidermal hyperplasia as being the factor responsible for the hardening and the thickening. From the histologic sections presented this does not appear to be the case. Whereas there is hyperkeratosis in one rather limited portion of the specimen, there is consistently in the corium a new growth of fibrous tissue in the subpapillary region around the plexus of the blood vessels, and that extends throughout the entire section. The changes there impressed me as analogous to those of a long-continued edema of the order of the edemas of elephantiasis nostras, and I am inclined to think that the stiffening of the part which is responsible for the xerosis is due to the fibrosis rather than to change in the epidermis.

DR J V KLAUDER. This condition recalls ocular pemphigus, better called essential shriveling of the conjunctiva or, still better, pemphigus of the mucous membranes. In that disease the mucous membranes become shriveled, adherent and obliterated. I have seen partial obliteration of the urethra of a woman, though never of the urethra of a man. Many times the disease remains localized in one mucous membrane, namely, the conjunctiva. Until more is known about the cause of both diseases, it is not unreasonable to consider the condition under discussion as related to ocular pemphigus.

Pemphigus of Long Duration in the Mouth, with Acute Exacerbation on the Skin, Improvement Following Large Doses of Vitamin D. Presented by DR THOMAS BUTTERWORTH, Reading, Pa.

G E F, a white man aged 63, presents many superficial ulcers on the palate, buccal mucosa, lips, tongue and throat. There are a few crusted lesions on the extremities. There is residual pigmentation at the sites of previous lesions on the trunk and extremities. The patient has had ulcers in his mouth since March 1938. A diagnosis of "trench mouth" was made, and he was given a course of treatments with neoarsphenamine. All the teeth were extracted before December 1938. He has been on a soft diet subsequently, with very little meat. About July 26 many unilocular blebs developed on various portions of the trunk and extremities. The patient had been a butcher, he had retired two years before the onset of the disease. The urinalysis gave negative results. A blood count showed 85 per cent hemoglobin, 4,500,000 erythrocytes and 13,100 leukocytes per cubic millimeter, color index 0.9 plus, 52 per cent polymorphonuclear leukocytes, 31 per cent small monocytes and 17 per cent eosinophils. The blood culture gave negative results. The sugar content of the blood was 83 mg and the urea nitrogen content 16 mg per hundred cubic centimeters. Culture of a bleb showed *Staphylococcus aureus*. The Wassermann reaction of the blood was negative. The stomach contents showed no free hydrochloric acid, but after histamine the value of hydrochloric acid was 66 and of total acid 91. Sulfanilamide in large doses was tried without improvement. There was a favorable response to administration of 400,000 units of vitamin D daily, together with ultraviolet irradiation and potassium permanganate baths.

DISCUSSION

DR A STRAUSS. I have tried vitamin D in a number of cases and have found that the treatment is highly satisfactory if the patient's health is good or if he is young enough to show some type of resistance. In older people who have acute pemphigus I have not observed good results. This case is striking in that the patient is a rather old man, although his general health is good. Seven or eight years ago, when I started using vitamin D therapy, I had 2 young patients, who have entirely recovered, but it caused no improvement in any of the older ones.

DR J M SCHILDKRAUT, Tinton, N J This man still has several active lesions in the mouth, so he may have some relapses I had one patient who was hospitalized for about fourteen months and in whom the condition finally cleared entirely under large doses of sulfanilamide

Reticulated Pigmented Poikiloderma of the Face and Neck (Civatte)

Presented by DR REUBEN FRIEDMAN

J P, a white man aged 46, presents a reticulated, reddish brown pigmentation on the forehead extending in an irregular bandlike fashion horizontally across the forehead and downward on each temple to and across the temporal hairline, where it abruptly ends Similar pigmentation of the skin is noted on the middle of the posterior aspect of each ear and also on the lateral aspect of the neck below the mastoid and in the region of the angle of the jaw The eruption also extends forward on each side involving part of the neck and the mandibular region Here and there within the area of involvement on the forehead are small irregular whitish atrophic patches and minute telangiectases Virtually all the reddish color of the eruption disappears on diascopic pressure, but a faint brownish pigmentation persists The sides of the neck present a minute whitish pinpoint stippling, corresponding largely to the pilosebaceous orifices It is noteworthy that the skin of that part of the retroauricular region of the head which is protected and shadowed by the ear is entirely free and sharply demarcated from the rest of the pigmentary disturbance The eruption began about three years ago on the left side of the forehead as a small reddish brown spot about the size of a tackhead It then spread slowly to the left ear for about one year and then toward the right ear The condition is entirely asymptomatic There is no history of any undue exposure to actinic rays The blood tests for syphilis gave negative results Histologic examination of a section of skin removed from the left side of the neck disclosed atrophy of the epidermis, with flattening and diminution in the number of papillae and dilatation and hyperkeratosis of the follicular openings There was a well marked distribution of golden brown pigment in the basal cells and an occasional clump of pigment in the upper part of the cutis The upper half of the cutis showed mild edema and dilatation of the blood vessels Around some of the vessels there were clumps of deeply staining cells which resembled nevus cells, but they were without pigment

DISCUSSION

DR FRED D WEIDMAN Histologically, there were atrophy of the epidermis, hyperpigmentation and but few telangiectases Perhaps the specimen was not taken from a part of the skin which showed the telangiectasis to the best possible advantage

DR DONALD M PILLSBURY I think that the condition is fairly typical of the poikiloderma which was described by the French during the World War, and of the melanosis of Riehl described by the Germans, apparently associated with some nutritional disturbance It is somewhat unusual in that the forehead was also involved, but I believe that has been described

DR REUBEN FRIEDMAN Some authorities consider Civatte's disease a variety of the war melanosis of Riehl, otherwise known as melanodermatitis toxica lichenoides et bullosa The condition in this case, however, differs from the latter at least in that Riehl's melanosis has a histologic picture strongly resembling lichen planus hence the use of the term lichenoides in the title given to that entity This particular section shows no cellular infiltration in the upper part of the cutis, as would be consistent with a lichen-planus-like picture Although they are separate and distinct entities, the Civatte type of poikiloderma may be regarded as one of a group of dermatoses of which Riehl's melanosis is the generic type

A Case for Diagnosis Localized Bullous Eruption with Keloidal Scarring
(Dermatitis artefacta?) Presented by DR DONALD M PILLSBURY

J H, a white girl aged 15, presents a widespread lesion involving the extensor surface of the right wrist and the dorsal surface of the hand, the upper portion consisting of a hypertrophic, somewhat tender scar and the lower, advancing portion being an oozing secondarily infected area at the site of the coalescent bullae. Swelling of the hand was noted originally, but this has subsided. There is no associated lymphangitis or lymphadenopathy. The rest of the cutaneous surface and the mucous membranes are normal. The vulva was not examined. The patient stated that in June a piece of smouldering rubber came in contact with her right wrist while she was burning some trash. About two hours later a small bulla was noted. Since that time a recurrent crop of ovoid and circular bullae has appeared at the lower portion and sides of the lesion. Scarring at the upper portion has gradually become more keloidal and tender. The history is somewhat contradictory as to whether or not complete healing has occurred since



Localized bullous eruption with keloidal scarring

the onset of the lesion. A fixed gelatin dressing was applied on October 13, and the borders of the lesion were outlined with carbolfuchsin. On removal of the fixed dressing on October 18, no extension of the process was noted. A tannic acid and merthiolate jelly was applied, and the hand and wrist were again enclosed in a fixed dressing. There is no history of drug ingestion. The blood count was normal. A culture of the contents of an intact bulla taken on October 9 remained sterile. The patient has received ultraviolet therapy and a wide variety of local applications, without particular effect on the progress of the lesion. A total of 140 r of roentgen rays in two doses, unfiltered, at 90 kilovolts, has been given.

DISCUSSION

DR J M SCHILDKRAUT, Trenton, N J I think that the process is a dermatitis artefacta.

DR J V KLAUDER Most patients with this condition have a hysterical make-up. Has this patient been examined for palatal and conjunctival anesthesia?

DR DONALD M PILLSBURY I have not made inquiry on that point.

NOTE—The lesions completely healed under occlusive dressing.

Book Reviews

A Text-Book of Occupational Diseases of the Skin By Louis Schwartz, M.D., Medical Director, United States Public Health Service, in Charge of Dermatoses Investigations, Washington, D. C., and Louis Tulipan, M.D., Clinical Professor of Dermatology and Syphilology, New York University College of Medicine, New York Price, \$10.00, cloth Pp 799, with 116 illustrations Philadelphia Lea & Febiger, 1939

This textbook of industrial dermatology is most welcome. Dermatologists, industrial physicians and others interested in the cause, prevention and treatment of dermatoses due to various irritants to which workers are subjected in various trades, occupations and professions will approve of a most adequate presentation of this rather neglected subject. Schwartz, because of his position in the United States Public Health Service, has been able to draw from his rich experience in industrial dermatology as could no other American dermatologist. He has been ably assisted by his co-author, Tulipan, who has also had intensive experience with industrial dermatoses in compensation work. While most of the material is drawn from the authors' own observations and experience, they have incorporated the reports of numerous other investigators in this field and have included an extensive list of references.

The first 74 pages are devoted to such subjects as the relation of workmen's compensation laws to dermatoses in the United States and the incidence and classification of causes of industrial diseases of the skin. There are chapters on the diagnosis and general methods of treatment and prevention. In the chapter on diagnosis of occupational dermatitis, patch tests are discussed together with the technic of patch testing and the interpretation of the results. A list of substances for patch tests, with the concentrations to be employed, is included.

In the main portion of the book the manufacturing processes and the chemicals used in industry are presented. Not only the chief substances which are likely to cause irritation of the skin in the manufacture of a certain product are listed but also the possible irritating qualities which may develop from the use of the final product. For instance, the various substances which may produce a dermatitis encountered in the manufacture of wool, silk, rubber goods, leather and cosmetics are given, as are also the many ways in which a dermatitis may develop in the users of the finished products.

Dermatoses caused by animal parasites, bacteria and fungi are adequately described, as well as occupational diseases of the mouth and nails. The authors give an analysis of the cutaneous hazards in seventy-four occupations. They include a list of "chemicals which are known to be or which can be skin irritants."

Some may feel that the size of the book could be materially reduced by eliminating seemingly nonpertinent descriptions of various industrial processes. The authors have sensed this and state "Although many details may appear irrelevant, such descriptions give the background on which the actual dermatosis develops, and make for a fuller understanding. In addition, they often aid in determining the possible irritants to which a worker may be exposed."

It is admitted that some of these descriptions seem rather nonessential, but they do serve as an important source for reference material.

All dermatologists and others interested in occupational diseases of the skin will feel indebted to the authors for the fulfillment in such an acceptable manner of a long-felt need.

Tumors of the Skin, Benign and Malignant Dr. Joseph Jordan Eller Price, \$10.00 Pp 607, with 403 illustrations Philadelphia Lea & Febiger, 1939

The author has written the first comprehensive treatise on benign and malignant tumors of the skin, including diagnosis and methods of treatment. The subject

of the benign tumors includes those of connective tissue origin, those originating from muscle and nerve tissue, nevi and other anomalies of the skin, tumors of infectious origin and precancerous conditions of the skin. Malignant tumors include carcinoma, malignant melanomas, sarcoma and lymphomas. A chapter on cutaneous surgery and plastic repair of tumors of the skin is also included.

An appendix contains practical data on radiation physics and biology, with dosage, and there are numerous tables and charts to determine the proper method of treatment and the proper dosage. An adequate bibliography has been included.

Both the clinical photographs and the photomicrographs are carefully selected and splendidly reproduced. With few exceptions they are unusually good. The only criticism to offer is that some of them which show effects of treatment are out of focus or too indistinct to be of value. Throughout the entire volume heavy glazed paper is used, which greatly aids the excellence of the reproductions.

It is a pleasure to read a book that is written in such a clear style, with no unnecessary verbiage and with a minimal discussion of debatable subjects. The book should prove of great interest to all dermatologists and to many practitioners.

News and Comment

DEATHS

Dr. Laurence R. Taussig, of San Francisco, died on February 11.

Dr. George M. Fisher, of Utica, N. Y., died on February 25.

Directory of Dermatologic Societies *

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Place New York Time Postponed indefinitely

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date

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METASTASES OF THE SCALP SIMULATING TURBAN TUMORS

F RONCHESE, M D

PROVIDENCE, R I

The case herein reported is interesting because of the rarity of cancerous metastases to the scalp and because of their striking similarity to turban tumors (figs 1 and 2). The rapidity of the development of the condition, which was the most important factor in the clinical diagnosis, was overlooked because of the decided resemblance, and the correct diagnosis of metastases was made only at the autopsy table.

Turban tumors is a short clinical name which designates a variety of slow-growing nonkeratinizing or basal cell epithelioma. It is characterized by multiple tumors varying in size from that of a pinhead to that of a pigeon's egg or larger and numbering from a few to hundreds. The tumors are usually confined to the scalp and are grouped in bunches, sometimes covering the entire scalp like a turban. The condition may be considered as an ultimate stage of adenoma sebaceum and epithelioma adenoides cysticum. This is also the opinion of Savatard¹ and others.

The development of turban tumors (fig 2) takes decades. In spite of the peculiar appearance of the growths, no patient ever died from them, and no excised tumors ever recurred. Hence the more detailed definition multiple benign epithelioma of the scalp (turban tumors).

After my review of the subject in 1933,² the name multiple benign epithelioma of the scalp was accepted by Andrews³ and was modified by Nékám⁴ as epithelioma benignum multiplex (Ancell). The Suttons,⁵

From the Department of Dermatology of the Rhode Island Hospital.

1 Savatard, L. Epithelioma Adenoides Cysticum, *Brit J Dermat* 50 333, 1938.

2 Ronchese, F. Multiple Benign Epithelioma of the Scalp (Turban Tumors), *Am J Cancer* 18 875, 1933.

3 Andrews, G C. Diseases of the Skin, ed 2, Philadelphia, W B Saunders Company, 1938, p 708.

4 Nékám, L. Deliberationes Congressu dermatologorum internationalis IX, Leipzig, Johann Ambrosius Barth, 1938, vol 5, pt 3, p 679.

5 Sutton, R L, and Sutton, R L, Jr. Diseases of the Skin, ed 10, St Louis, C V Mosby Company, 1939, pp 678 and 813.

in the 1939 edition of their textbook on cutaneous diseases, changed the classification from the basal cell epitheliomas to the still more benign syringomas

From my survey of the literature in 1933,² it is clear that Ancell in 1842 was the first author to describe a case of turban tumors. I cited

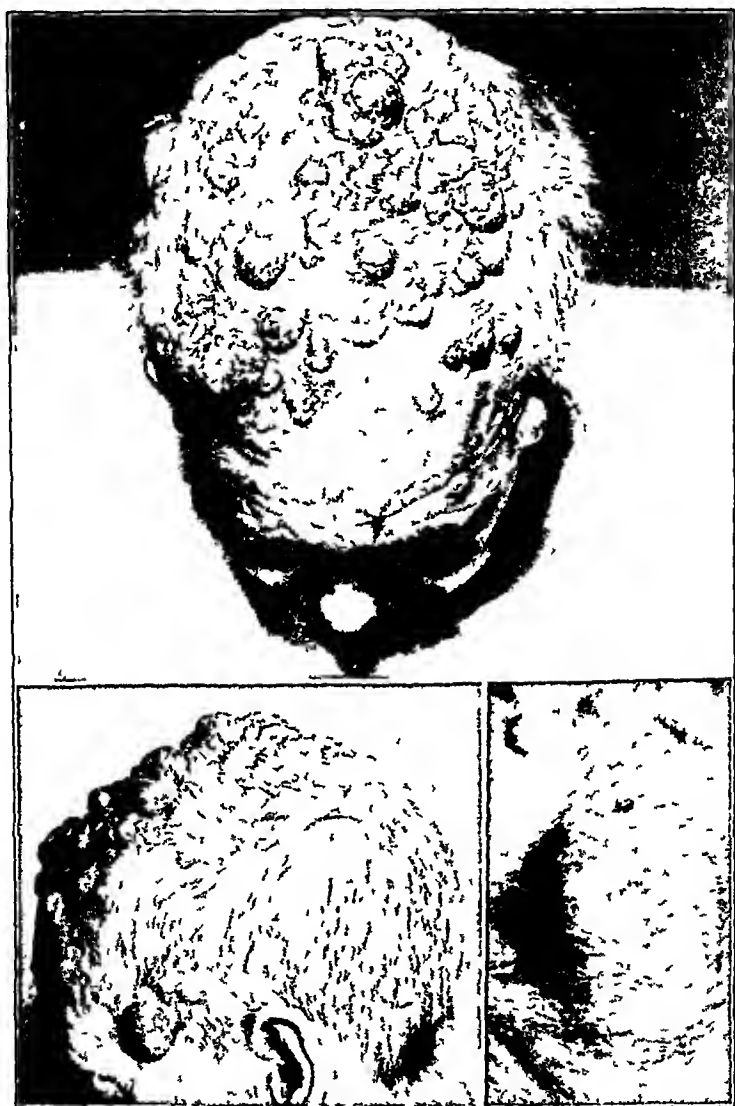


Fig 1—Metastatic tumors from a carcinoma of the prostate which developed in sixteen months, involving the scalp, with practical exclusion of the rest of the cutaneous surface

and discussed 31 cases which had appeared in the literature since the publication of Ancell under various names and interpretations, such as endothelioma capitis of Kaposi, Spiegler's tumors, cylindroma of the scalp, syphonoma and tomato tumors. At present 13 more cases of turban tumors can be added (Guimarães Porto, Snoke and Belk,

Stillians, Schlamadinger, Hval, Schuermann and Weber, Binkley; Nicholson and Becker, Zakon)⁶ Two of these were previously overlooked, while the others have been published since 1933, making a total of 44 (24 patients were women, 20, men) The condition in Zakon's case is one of the clearest and most typical examples of the tumors fully developed I hope that authors of textbooks on surgery will introduce turban tumors to the surgeons



Fig 2—Clinical appearance of turban tumors (case reported by Ronchese²) resembling those in figure 1

REPORT OF A CASE

I N, an American aged 69, entered the Rhode Island Hospital on Sept 1, 1937 He had been under osteopathic care for a long time with rheumatic arthritis and had been under medical observation for six months He was a pale, emaciated elderly man, lying flat in bed, complaining of pains in his abdomen and joints, including the phalangeal joints, ankles and elbows and especially the shoulder and hip joints

6 Guimarães Porto, A Tumores confluentes do couro cabelludo (Adenomas sebaceos), Arch brasil de med 2 699, 1912 A moulage of this case was presented to the Paris Surgical Society and is reproduced in its bulletin (Auvray Tumeurs

His blood pressure was 90 systolic and 40 diastolic. His temperature, pulse and respiration were normal. The Wassermann reaction was negative. Examination of the blood showed hemoglobin between 60 and 65 per cent, erythrocytes about 3,000,000 per cubic millimeter and leukocytes between 8,100 at first and 18,000 toward the end. Chemical examination of the blood showed urea nitrogen between 22 and 15 mg, cholesterol 220 mg, creatinine 1.2 mg and dextrose from 74 to 82 mg per hundred cubic centimeters. The Mantoux test, with a dilution of 1:1,000, gave a negative result. The urine was normal at first and then showed gradually increasing albumin. The sediment showed a progressive increase in white and red blood cells.

The family history was irrelevant. No members had tumors of any kind.

The patient's scalp was literally covered with fairly mobile firm pink tumors (fig 1), which ranged in size from that of a pea to that of a walnut. They were grouped together and had fairly smooth surfaces, some being slightly pedunculated. Some were slightly tender. Some were of rubber consistency. Those on the side of the head, covered by normal skin, had large follicular openings, resembling the outer surface of a strawberry. The patient paid no attention to them, evidently on account of the pain he was suffering elsewhere.

I saw the patient for the first time in April 1938. He stated emphatically that in January 1937, or sixteen months previously, his bald head was as smooth as a billiard ball. This statement was confirmed by a physician who had seen him in consultation late in 1936.

The growths began to appear at about that time and increased rapidly in number and in size. At the time the picture was taken (fig 1) the largest tumors were only sixteen months old, while the pea-sized nodules were about one month old. Half a dozen, also pea-sized ones, were scattered on the thorax, back and abdomen. The rest of the cutaneous surface was free from tumors.

No neurologic symptoms were present.

There was a history of several months of acute cystitis, without bladder obstruction. Repeated rectal examinations showed no involvement of the prostate. Just prior to his admission an acute obstruction of the bladder developed, and a self-retaining catheter was inserted. Two weeks later rectal examination revealed that the acute inflammation had disappeared and that no evidence of malignant disease was present. Thereafter the catheter was changed every six to eight days. There was no acute pain in the bladder or prostate at any time, and the catheter

confluentes du cuir chevelu, par M. A. Guimarães Porto, Bull. et mem. Soc. nat. de chir. **61**: 284, 1935. Snook, P. O., and Belk, W. P. Multiple Primary Tumors of the Skin [case 1], S. Clin. North America **7**: 437, 1927. Stillians, A. W. Multiple Benign Epithelioma of the Scalp, Arch. Dermat. & Syph. **25**: 941 (May) 1932. Nevo-Epithelioma Adenoides (Cylindroma) of the Scalp, *ibid.* **27**: 481 (March) 1933. Schlamadinger, J. Cylindrom und Trichoepithelioma papulosum multiplex, Arch. f. Dermat. u. Syph. **171**: 526, 1935. Hval, E. Adenomata of Sweat-Glands and Other Kindred Tumours. Their Generic Relationship to Naevi [cases 10 and 11], Acta dermat.-venereol. **12**: 1, 1936. Schuermann, H., and Weber, K. Beitrag zur Kenntnis der Spieglerischen Tumoren (Cylindrome) nebst einigen Bemerkungen zum Epithelioma adenoides cysticum, Arch. f. Dermat. u. Syph. **175**: 682, 1937. Binkley, G. W. Naevus Epitheliomato-Cylindromatosus, Arch. Dermat. & Syph. **37**: 289 (Feb.) 1938. Nicholson, M. A., and Becker, F. T. Naevus Epitheliomacylindromatosus, *ibid.* **39**: 543 (March) 1939. Zakon, S. J. Naevopithelioma Adenoides Cylindromatosum of the Scalp, *ibid.* **40**: 626 (Oct.) 1939. Naevopithelioma Adenoides (Cylindroma) of the Scalp, *ibid.* **40**: 945 (Dec.) 1939.

was easily introduced, with no evidence of obstruction. Rapid formation of crystals in the urine was noted. Roentgen examination of the chest, pelvis and long bones showed no pathologic changes.



Fig 3—Gross and lower power microscopic appearance of metastatic tumors of the meninges

The treatment consisted of subcutaneous injections of a solution of a bacterial antigen and administration of liver extract, vitamin B complex, iron and sedatives to ease the gradually increasing discomfort. There were several transfusions of blood.

On April 21, 1938, a tumor was removed for histologic examination, the diagnosis being nonkeratinizing epithelioma.

The same day fourteen 1 mg radium needles were inserted in a mass of tumors about the patient's forehead and were left in place for one week. On an area of approximately 4 by 4 cm, above the bregma, 250 mg of radium, in seven tubes, with an 0.5 mm platinum filter, was placed at 2 cm distance from the skin and was left in place for eight hours.

On June 1, in areas where the needles had been inserted the tumors had practically disappeared, and where the radium tubes had been applied the tumors were greatly reduced in size.

The area from which the biopsy specimen was taken healed by primary union in about one week. The patient grew progressively worse and died on June 6. The diagnosis on discharge was osteoarthritis.

The autopsy showed a primary carcinoma of the prostate, with extension to the seminal vesicles. Metastatic lesions extended to the lungs, lymph nodes, adrenals, dura mater (fig 3), skull, accessory nasal sinuses, bones and skin of the chest, abdomen, back and scalp.

There were calculi of the renal pelvis and bladder, hypertrophy of the bladder, hydroureter, hydronephrosis, chronic cystitis, ureteritis, pyelonephritis and acute epididymitis.

Microscopic sections of the prostate and of metastatic tumors (figs 4 and 5) confirmed the diagnosis of primary and metastatic carcinoma.

COMMENT

While metastases to the lymph nodes and internal organs are frequent, metastases to the skin are infrequent, and cutaneous metastases on the scalp are rare.

Cutler, Buschke and Cantil⁷ stated

There are certain barriers which a malignant growth may encounter in its spread. These may be in the form of a dense fibrous tissue, periosteum or perichondrium. The selection of metastatic sites which certain tumors seem to exhibit cannot be explained by anatomic considerations alone but must have some relation to the biologic affinity of certain forms of growth for a particular soil.

Metastases to the scalp do not have to go necessarily through the skull. Cases with widespread metastases to the skin but not to the scalp are as mysterious as the present one, with widespread metastases to the scalp and practically none to the rest of the cutaneous surface.

Willis⁸ mentioned a few reports of cases in which metastases to the scalp occurred. They were mostly represented by a small solitary nodule or by a few small ones. He said that he had seen a solitary metastasis

⁷ Cutler, M., Buschke, F., and Cantil, S. T. *Cancer: Its Diagnosis and Treatment*, Philadelphia, W. B. Saunders Company, 1938.

⁸ Willis, R. A. *The Spread of Tumours in the Human Body*, London, J. & A. Churchill, 1934.

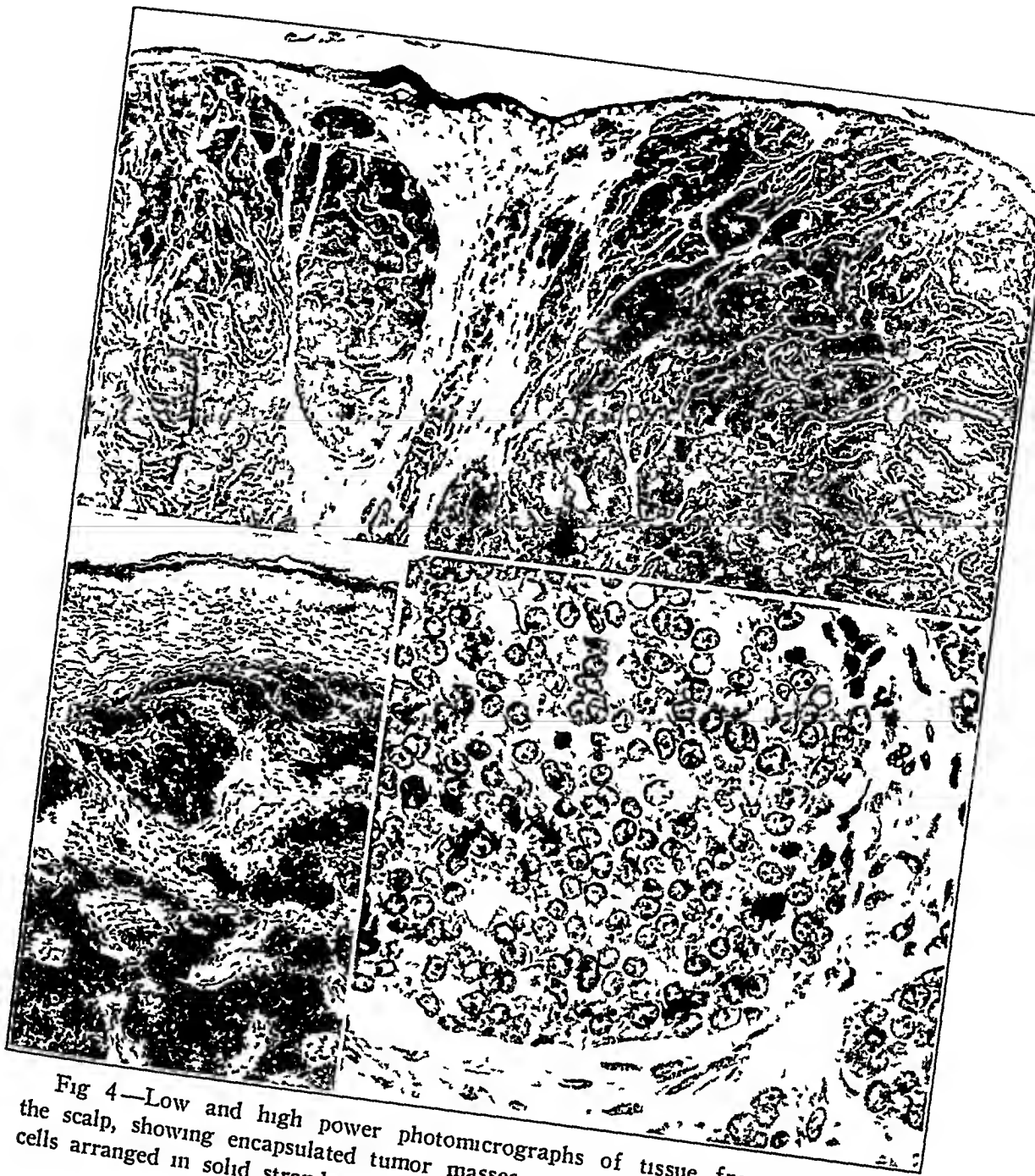


Fig 4—Low and high power photomicrographs of tissue from tumors of the scalp, showing encapsulated tumor masses, made up of polygonal epithelial cells arranged in solid strands or in nests or diffusely scattered

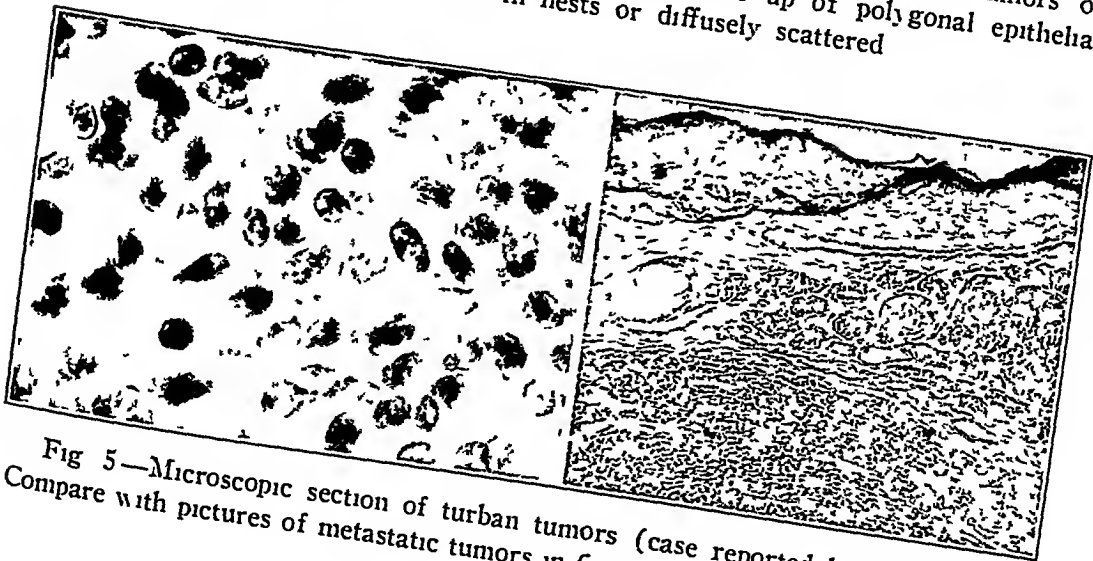


Fig 5—Microscopic section of turban tumors (case reported by Ronchese²) Compare with pictures of metastatic tumors in figures 3 and 4

of the scalp from a mucoid carcinoma of the colon Kaufmann-Wolf,⁹ among 65 cases of cutaneous metastases, mentioned 1 case in which the scalp was involved

Symmers,¹⁰ among 298 cases of malignant tumors, of which 220 showed metastases, reported that in 3 cases a solitary metastatic tumor was located on the scalp Small metastatic nodules on the scalp were reported by Goldsmith¹¹ in a 70 year old woman, in whom, subsequently, a carcinoma of the breast was found A solitary nodule of the scalp was reported by Robinson and Castleman¹² in a case of benign metastasizing hemangioma This "benign" growth, however, caused the death of the patient in twenty-one months Fay and Henry¹³ reported a case of subcutaneous metastatic nodule of the scalp from a hypernephroma The authors studied the relation of the temperature of the body to metastasis and particularly of the temperature of the skin in segments of the body Metastases are favored by warmth, and the head and neck were found to be the warmest parts of the body

In Sutton and Sutton's⁶ book there is a good illustration of multiple metastatic tumors of the scalp from a hypernephroma It seems that the scalp is a preferred site of metastasis from a primary cancer of the genitourinary tract Graves,¹⁴ summarizing a statistical study, stated that in cases of hypernephroma it is not uncommon to find a metastatic tumor before there are any symptoms referable to the genitourinary tract He mentioned the scalp as a location of the rapidly metastasizing tumors

The statistics of Broders¹⁵ showed many metastases of the lymph nodes but few of the skin and none of the scalp

9 Kaufmann-Wolf, M Klinische und histologische Beobachtungen bei Haut-metastasen im Anschluss an Karzinom innerer Organe, *Arch f Dermat u Syph* **114** 709, 1913

10 Symmers, D The Metastasis of Tumors A Study of Two Hundred and Ninety-Eight Cases of Malignant Growth Exhibited Among 5,155 Autopsies at Bellevue Hospital, *Am J M Sc* **154** 225, 1917

11 Goldsmith, W N A Case of Metastatic Scirrhus Carcinoma of the Scalp, *Brit J Dermat* **41** 270, 1929

12 Robinson, J M, and Castleman, B Benign Metastasizing Hemangioma, *Ann Surg* **104** 453, 1936

13 Fay, T, and Henny, G C Correlation of Body Segmental Temperature and Its Relation to the Location of Carcinomatous Metastasis Clinical Observations and Response to Methods of Refrigeration, *Surg, Gynec & Obst* **66** 512, 1938

14 Graves, R C Analysis of Cases at the Pondville Hospital Cancer of the Genito-Urinary Organs, *Am J Cancer (supp)* **15** 2393, 1931

15 Broders, A C Squamous-Cell Epithelioma of the Lip A Study of Five Hundred and Thirty-Seven Cases, *J A M A* **74** 656 (March 6) 1920, Squamous-Cell Epithelioma of the Skin, *Ann Surg* **73** 141, 1921, Epithelioma of Cavities and Internal Organs of the Head and Neck, *Arch Surg* **11** 43 (July) 1925

Keeney ¹⁶ reported an interesting case of carcinoma of the trachea metastasizing to internal organs and to the skin. The trunk of the patient was showered with tumors, but none appeared on the scalp.

So far as I know, the only case of extensive metastases to the scalp, a replica of my reported case of turban tumors ² (fig 2), is the one of Sequeira ¹⁷. The metastatic tumors spread rapidly from a chondrosarcoma of the foot, which was amputated four years previously. However, Dr Sequeira kindly informed me that he had no knowledge of the outcome of his case.

Metastatic tumors diagnosed as such only at the autopsy table are not exceptional.

Symmers ¹⁸ cited a case of metastatic tumors clinically diagnosed as Recklinghausen's disease.

The condition in Goldsmith's ¹¹ case was undiagnosed for a long time, until the carcinoma of the breast was discovered. In Way and Light's ¹⁸ case of rapid generalized melanosis three or four minute lesions on the scalp were the first evidence of metastasis but were not recognized as such. They were followed by a shower of metastatic lesions involving the entire body, which closely simulated purpura haemorrhagica and were diagnosed as such for a while by numerous physicians.

Montgomery ¹⁹ stated that he had encountered 2 cases in which the cutaneous metastatic lesions were limited to the scalp and misdiagnosed as sebaceous cysts or benign sweat gland carcinomas because the primary carcinoma of the gastrointestinal tract had not yet become extensive enough to be recognized by clinical or laboratory signs.

In the present case I considered the emaciation of the patient as consistent with the age and the long-standing rheumatic arthritis and cystitis. I did not give due consideration to the most important fact, viz., such an extensive involvement of an area of the body in only sixteen months. Even though the grouping of such a large number of tumors in such a location is extremely rare and its appearance in this case was so strikingly similar to turban tumors, the rapidity of its evolution should have ruled out such a diagnosis. The absence of tumors in members of the family was also contrary to the diagnosis of turban tumors. The fact that the patient did not pay attention to his scalp, because of much suffering elsewhere, was misleading, as was the histologic diagnosis of the sections from one of the tumors.

16 Keeney, E. L. Primary Carcinoma of the Trachea with Cutaneous Carcinomatosis, *Bull Johns Hopkins Hosp* 61:411, 1937.

17 Sequeira, J. H., and Turnbull, H. M. Sarcoma of the Skin, & c., Secondary to Tumour of the Foot, *Proc Roy Soc Med (Sect Dermat.)* 8:8, 1914.

18 Way, S. C., and Light, S. E. Generalized Melanosis. Report of a Case with Necropsy, *J A M A* 94:241 (Jan 25) 1930.

19 Montgomery, H. Early Recognition and Treatment of Skin Cancer, *S Clin North America* 17:1249, 1937.

One must be prepared to recognize the occurrence of metastatic carcinoma resembling a basal cell epithelioma. The difficulties often met in reaching a pathologic diagnosis are not surprising. Cutler, Buschke and Cantril⁷ said

The histologic structure of a metastatic growth is sometimes more typical of the tumor from which it has arisen than is the primary lesion itself. There are forms, however, in which the metastases do not resemble the tumor from which they have arisen and the clinical rather than the histologic considerations must guide the diagnosis and management.

SUMMARY

A case of unusually extensive metastases to the scalp from a carcinoma of the prostate is reported.

The case is interesting because of the rarity of metastases to the scalp and because of the extreme rarity of the occurrence of such a large number of tumors grouped in one area of the body while practically none were located on the rest of the cutaneous surface.

The case is interesting also because of the striking similarity of the condition to turban tumors, both clinically and histologically. This similarity was the cause of the diagnostic error which was corrected at the autopsy table.

122 Waterman Street

A NEW MODIFICATION OF THE PATCH TEST (THE CHAMBER METHOD)

INGVALD ROKSTAD, M D

OSLO, NORWAY

Since the so-called patch test (J Jadassohn, B Bloch) has been adopted widely for examination of eczema, various authors have suggested modifications of the technic, lately with a view to particular purposes (Rattner¹, Guild²)

In the dermatologic department of the Finsen Institute, systematic studies have been carried out since the autumn of 1938 on the non-specific (i e., caustic) effect of various terpenes on the skin To begin with, the same method was employed as is used in this institute for eczema tests A strip of boiled linen, an impermeable layer of cellophane and adhesive tape for fixation are used, up to six tests being performed on the same strip. The result is read after twenty-four hours, and a control reading is made on the following days (Bonnevie³)

The first examinations gave paradoxical results For instance, the same concentration of a substance, such as 100 per cent alpha pinene, gave in some persons a maximal reaction (purulent bulla) and in others a perfectly negative reaction Moreover, on repetition of the test on the same persons, results widely divergent from the first ones could be observed Often the reactions were inversely proportional to the concentrations employed, a low concentration giving a stronger reaction than a high concentration

As the differences in these results could not be ascribed to individual differences in the properties of the skin, it seemed reasonable to attribute them to defects in the method employed for the tests (largely to insufficiency of the so-called impermeable layer), enabling the volatile test substances to escape This was strongly suggested by the fact that in the first hours after their application the test patches gave off a strong odor, which subsided gradually

Negative reactions (or simply absence of reactions) were met with regularly in tests in which the tape had formed folds so that the cello-

From the Department of Dermatology, Finsen Institute (Prof Svend Lomholt)

1 Rattner, H A Device for a "Continuous" Patch Test, Arch Dermat & Syph 38:619 (Oct) 1938

2 Guild, T B Window Patch Test, Arch Dermat & Syph 39:807 (May) 1939

3 Bonnevie, P Aetiologie und Pathogenese der Ekzemkrankheiten, Copenhagen, Nyt Nordisk Forlag Arnold Busck, 1939, p 55

phane sheet did not fit tightly to the skin. However, such reactions were observed also in tests in which the patch apparently was fitting snugly.

These two circumstances suggested that the test substances might escape not only through leaks between the cellophane plate and the skin but also directly by diffusion through the cellophane plate. These shortcomings were not so conspicuous with pinene-hypersensitive persons, on whom the tests were made with lower concentrations and the test material consisted largely of a nonvolatile substance, namely, olive oil (less evaporation).

Experiments were made, therefore, with modifications of the impermeable layer, the sheet of cellophane being replaced by a somewhat thicker plate, of celluloid. This plate, however, did not enclose the

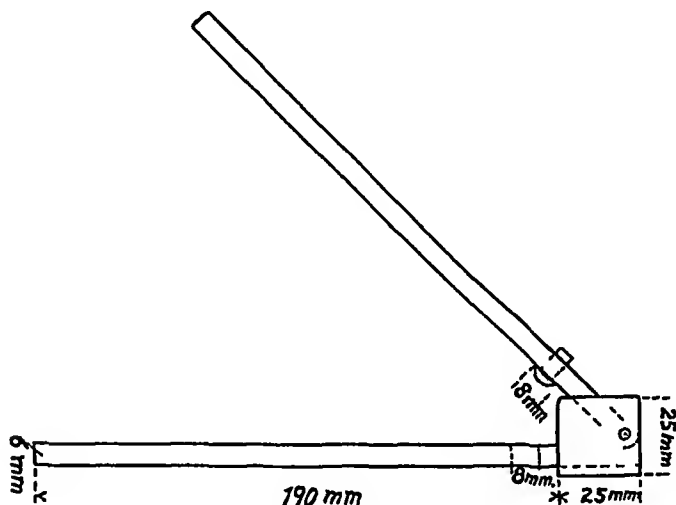


Fig 1—Forceps for production of the chamber

patch as well as did the cellophane sheet, it rather exerted pressure on the test patch, so that the substance in use was forced out along the margin, where some of it escaped. In order to avoid this the center of the plate was transformed into a chamber, so that no pressure was exerted on the test patch.

This chamber was obtained by pressing the celluloid plate with a forceps resembling a nutcracker (fig 1), one arm of which had a circular hole 8 mm in diameter, while the other was equipped with a circular knob that fitted into this hole. These celluloid chambers will soon be manufactured commercially.

THE CHAMBER METHOD

After numerous experiments with various chambers the most appropriate device was selected (fig 2).

The chamber is circular, with a roundish top, it is surrounded by a flat marginal plate. The diameter of the chamber is 8 mm, and its central height, measured from the inferior surface of the marginal plate (external measurement), is 1.8 mm. The celluloid plate is square, each side measuring 18 mm in length and 0.3 mm in thickness.

The transformation of the impermeable layer from a plate to a chamber brings about an effect entirely different from that of the former arrangement, as it not only prevents escape of the volatile test substances but exerts a special effect on the skin.

When the patch is removed after twenty-four hours and the concentration employed has not been strong enough to give a reaction, the skin shows a platelike elevation corresponding to the lumen of the chamber, pale and firmly infiltrated. It is like an urticarial wheal or papule, or like the site of a recent intracutaneous injection. It disappears within half an hour.

This "papule" is to be looked on not as a product of pressure but rather as the opposite, a result of suction.

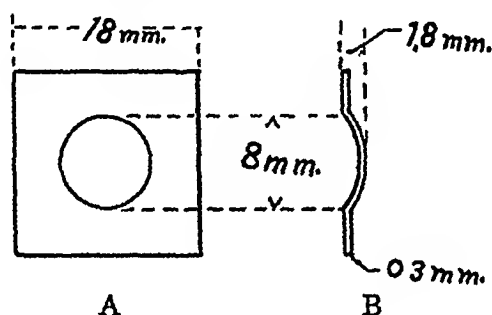


Fig 2—A, chamber seen from above, B, chamber seen from the side

As the patch test is applied, the skin is pressed up into the chamber so that all air is forced out. (At the same time a little of the test fluid is forced out between the collar plate of the chamber and the underlying skin, making the connection more air tight.) After application of the adhesive tape the chamber is fixed firmly, yet the skin in the chamber is able to retract somewhat on account of its elasticity. This gives a negative pressure in the chamber and a corresponding suction effect on the skin, which not only prevents the skin from retracting entirely from the chamber but causes this area of the skin gradually to be infiltrated with the tissue juice.

A condition for the establishment of this suction effect is that the height of the chamber be not too low, that the marginal plate around the chamber be not too narrow and the tape sufficiently sticky. A very low chamber will have only a slight suction effect, and a very narrow marginal plate may easily release the firm hold on the skin so that air invades the chamber again. In applying the patch a slight pressure

is to be exerted, and the skin must fill the chamber before the adhesive tape is put on

Figure 3 illustrates the chamber ready for application (with patch and tape), its application to the skin and a papule seen immediately after removal from the chamber

Now and then the papule may be absent or inconspicuous (merely a mark of pressure) This is due to the circumstance that a suction effect was not obtained or soon ceased In such cases the method yields no more than does the ordinary patch test and the result is to be considered a failure

The papule is the criterion of a successful test A pale papule means a truly negative reaction, whereas the absence of a papule indicates a failure of technic and requires repetition of the test

The pale papule can never be misinterpreted as a positive reaction, as a positive reaction always produces definite changes on the surface

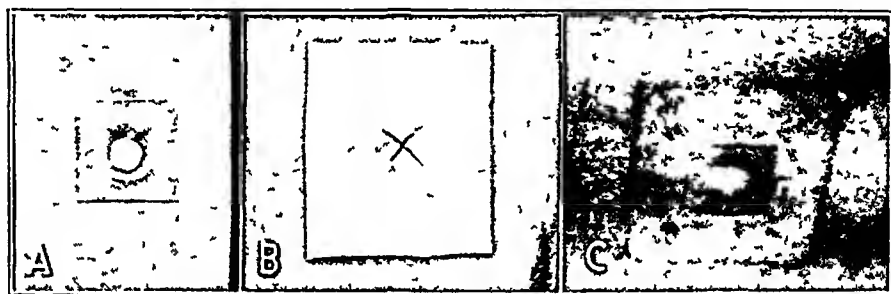


Fig 3—A, chamber ready for use (mounted on the tape, and with the patch in place) B, chamber applied to the skin C, skin about ten minutes after removal of the chamber and patch The reaction is negative The papule is a criterion of the successful performance of the test

(such as redness, brownish pigmentation, scaling or pustules), according to the concentration employed and the reacting organism

Results of a comparative assay of the ordinary patch test and the chamber method with employment of volatile substances (so far only volatile substances have been employed for such tests) are in favor of the chamber method In general, the ordinary patch test gives fairly reliable results under favorable circumstances, but the outcome may readily be influenced by technical defects in the application of the test, and if several such defects happen to occur at the same time the result may be a complete failure of the test—without any evidence to this effect

The chamber method also may fail, i e., it happens now and then that no suction effect is obtained Then, however, the papule is absent too

As to the positive reactions with the method formerly employed, distinction is made between a minimal reaction (mere redness) and a

maximal reaction (purulent bulla) The minimal reaction may in rare cases appear in response to a concentration of 45 per cent and the maximal reaction to one of 75 per cent, but the appearance of positive reactions was more regular only with employment of higher concentrations, and the maximal reaction was often absent even on application of a 100 per cent solution

With the chamber method the same reactions commonly appear in response to concentrations of 30 and 60 per cent As far as the maximal reaction is concerned, it has been observed in a few cases even with a concentration of 45 per cent, and practically always before one of 100 per cent is reached

Probably the greater effectiveness of the chamber method is due to the circumstance that the chamber forms not merely a water-tight but also an air-tight space, from which the test substance may disappear only in the way that is intended, through absorption by the skin Furthermore, it is conceivable that the protective layer of horn and sebum on the skin is influenced by the suction effect of the chamber in such a way as to facilitate the permeation of the test substances, so that they more rapidly come in contact with the cells of the skin that react to their presence

SUMMARY

For examination of the nonspecific toxic (i.e., caustic) effect on the skin exerted by certain volatile substances (e.g., terpenes) the patch test method commonly employed in eczema tests is unreliable

A new method has been worked out, therefore, in which the cellophane plate (or impregnated cambric) is replaced by a celluloid chamber (fig 2), which is fixed to the skin with adhesive tape (or, in cases of hypersensitiveness to the tape, with a paste made with 15 Gm of zinc oxide, 15 Gm of gelatin, 25 Gm of glycerin and 45 cc of distilled water)

When applied correctly, the chamber exerts a suction effect on the skin, not merely providing an air-tight space that prevents escape of the volatile test substance but inducing the formation of a papule within a certain length of time (fig 3 C)

This papule, then, indicates that the suction effect has been present, in other words, it constitutes the criterion of a successful test technic Besides, the edematous condition of the papule may be assumed to facilitate the absorption of the test substances through the horny and sebaceous barrier of the skin

In studies on the toxicity (i.e., the caustic effect) of the terpenes, which will be published later, this method has given constant results, revealing lower threshold values than had been previously established for erythematous or for bullous (purulent) reactions

ANDROGENIC SUBSTANCE AND SWEAT

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AND

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The development of the pilosebaceous apparatus at puberty and the commonly believed association of some cutaneous diseases, such as acne, with the "sex hormones" prompt the belief that the skin is intimately influenced by these agents. It has been shown that preparations of these hormones when applied to the skin may be absorbed and have systemic action¹

When androgens are injected intramuscularly, only a part of the total can be recovered in the urine². Since the skin is so permeable to the substances from without inward, it seemed possible that route of excretion might be through the sweat. An investigation therefore was made to determine to what extent androgenic substances occurred on the surface of the skin or in the sweat and oil.

METHOD

The subjects were encased in a rubber sack as far as the neck and placed in a heat cabinet. Some were given 50 mg of testosterone propionate³ intramuscularly twenty-four or forty-eight hours previously. The amount of sweat collected varied from 70 to 125 cc. This contained cellular debris and sebaceous gland secretion elements. The collected material was acidified with one-tenth volume of hydrochloric acid. The mixture was shaken in a separatory funnel with a small quantity of ether (50 cc). After the two layers were separated, the ether was removed and the sweat extracted a second time with ether. The ether extracts were combined and concentrated to a small volume. Mazola (corn) oil (5 cc) was added and the last of the ether removed on a water bath under reduced pressure. The oil was assayed for androgenic content on 1 day old white leghorn chicks. Three birds were used for each preparation. Each received 0.2 cc daily for six days, and their combs were examined for any stimulation on

From the Department of Dermatology of the University of Illinois College of Medicine

The expenses for this investigation were defrayed by a grant from the Committee on Scientific Investigation of the American Medical Association

1 Kearns, W M. The Clinical Application of Testosterone, *J A M A* **112** 2255 (June 3) 1939

2 Hoskins, W H, Coffman, J R, Koch, F C, and Kenyon, A J. The Effect of Testosterone Propionate on the Urinary Excretion of Androgens and Estrogens in Eunuchoidism, *Endocrinology* **24** 702, 1939

3 The testosterone propionate (perandren) was furnished by the Ciba Company

the seventh day. A control series of tests was always run in which the chickens received 20 micrograms of crystalline androsterone⁴ in 0.2 cc of mazola (corn) oil daily. Out of 15 birds in the control series, sometimes 1 would fail to respond to this dose. The results of the tests on 7 human beings are shown in the accompanying tabulation.

| Patient | Treatment | Result |
|---------|--------------------|----------|
| D W | None | Negative |
| B S | None | Negative |
| M R | None | Negative |
| A M | 50 mg testosterone | Negative |
| J C | 50 mg testosterone | Negative |
| S C | 50 mg testosterone | Negative |
| D F | 50 mg testosterone | Negative |

J M, a normal white woman 35 years old, was caused to sweat at repeated intervals, at which times about 125 cc of sweat would be obtained. The specimens were preserved with chloroform in the refrigerator. A total of 2,000 cc was collected. Concentrated hydrochloric acid (200 cc) was added, and the mixture was boiled for fifteen minutes. It was then cooled and extracted with chloroform for forty-eight hours in a continuous extractor. The chloroform was evaporated and the residue taken up in ether. This was evaporated to a small volume and 5 cc of mazola (corn) oil added. The remainder of the ether was removed with vacuum in a water bath of boiling water. The oil was assayed on 3 white leghorn baby chicks, with uniformly negative results. Since the method would detect 0.36 mg of androsterone, it would appear that a negligible quantity was excreted in the 2 liters of sweat.

The method was tested for recovery by adding 5 mg of crystalline androsterone to a sample of sweat. One tenth of the volume of concentrated hydrochloric acid was added and the mixture extracted twice with a small amount of ether, the separatory funnel being used. The ether extract was put into mazola (corn) oil and assayed on 3 white leghorn baby chicks. All 3 gave a positive response. This indicates that the method would recover added androgen.

COMMENT

Thus far, most attempts at finding "sex hormones" in the sweat have ended in failure. Gilman and Weidman⁵ were unable to obtain a positive Aschheim-Zondek reaction with the sweat from a pregnant woman. Japanese investigators⁶ did not find evidence of estrogenic substance in the sweat. Garofalo,⁷ using the rabbit as test animal,

⁴ The crystalline androsterone was furnished by G. Stragnell, of the Shering Corporation.

⁵ Gilman, R. L., and Weidman, F. D. Perspiration. Absence of Aschheim-Zondek Hormone in Pregnancy, *Arch. Dermat. & Syph.* **25**:852 (May) 1932.

⁶ Kosako, J.; Okamoto, S., and Kosuge, T. Are Sexual Hormones Excreted in Sweat? *Jap. J. Obst. & Gynec.* **20**:279, 1937.

⁷ Garofalo, A. Presence of Pituitary Hormones in Sweat of Pregnant Animals, *Clin. Obst.* **36**:69, 1934.

obtained only negative reactions for gonadotropic substance. When the mouse was used he found only small quantities of gonadotropic substance irregularly. Consoli⁸ was able to confirm Garofalo's results. The present data show that there was no androgenic substance evident in as much as 2 liters of sweat.

It appears that appreciable quantities of the "sex hormones" are not regularly present on the surface of the skin or in the secretions found there. We have used these various factors locally on the skin in the treatment of acne and of several other dermatoses.

SUMMARY

No appreciable quantity of androgenic substance has been found in as much as 2,000 cc of sweat.

Androgenic substance was not detected in the sweat or on the cutaneous surface after intramuscular injection of large quantities of testosterone propionate.

⁸ Consoli, V. Prolan (Pituitary Preparation) in Sweat of Pregnant Women, *Clin obst* 36:80, 1934.

ROLE OF VITAMIN C IN VARIOUS CUTANEOUS DISEASES

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AND

JOHN H TALBOTT, M D

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The concentrations of vitamin C in the blood of 68 apparently healthy persons and in that of 181 patients seen in the dermatologic clinic are reported in this paper. The experimental data on both groups showed wide scattering. No significant correlation was noted in the second group between the concentration of vitamin C in the blood and the development of lesions of the skin. Large amounts of vitamin C¹ were given to selected patients, but no therapeutic effects were achieved.

The purpose of this study was confirmation or rejection of the presumption that a deficiency of vitamin C in the body is a contributory etiologic factor in the production of certain diseases of the skin. This presumption has been based on data obtained by several investigators from patients with psoriasis, urticaria, lupus vulgaris, lupus erythematosus, generalized exfoliative dermatitis and eczema. They observed in most instances a low level of vitamin C in the blood or a diminished excretion of this substance in the urine, and treatment with large amounts of vitamin C produced equivocal results.

PROCEDURE

The blood for determinations of vitamin C was taken in the morning from persons who had not consumed that day any food which contained vitamin C. A short dietary history was obtained at the same time. The determination on the blood was performed shortly afterward, by the macromethod described by Mindlen and Butler².

VITAMIN C IN APPARENTLY HEALTHY PERSONS

Literature—The level of vitamin C in the blood in apparently healthy persons varies over a great range. Abt and Farmer³ stated that

This investigation was aided by the Corn Industries Research Foundation.

From the Dermatological and Medical Clinics of the Massachusetts General Hospital and the Fatigue Laboratory, Harvard University.

1 Merck and Co. supplied the vitamin C used in this study.

2 Mindlen, R. L., and Butler, A. M. Determination of Ascorbic Acid in Plasma. Macromethod and Micromethod, *J Biol Chem* **122**:673, 1938.

3 Abt, A. F., and Farmer, C. J. Vitamin C. Pharmacology and Therapeutics, *J A M A* **111**:1555 (Oct 22) 1938.

"in healthy individuals on what is considered an adequate vitamin C intake the blood plasma value will be 0.7 mg per hundred cubic centimeters or above. Blood plasma values below 0.7 mg per hundred cubic centimeters are subnormal or at least suboptimal. Active scurvy may occur with values ranging up to 0.4 to 0.5 mg. per hundred cubic centimeters." King⁴ stated the belief that a normal concentration is above 1 mg per hundred cubic centimeters, that 0.8 mg is low and that with 0.5 mg scurvy may develop. Ingalls⁵ summarized the vitamin C values in the blood of a series of children as follows (values represent milligrams per hundred cubic centimeters)

| | |
|---------------------|-----------|
| Optimum | |
| Saturation | 2.00-1.00 |
| Normal | 1.00-0.70 |
| Low normal | 0.70-0.50 |
| Suboptimum | 0.50-0.30 |
| Deficiency | |
| Asymptomatic scurvy | 0.30-0.15 |
| Scurvy [clinical] | 0.15-0.00 |

Trier,⁶ of Copenhagen, Denmark, in observing a large group of normal persons, found that the vitamin C level in the summer ranged between 0.30 and 0.50 mg per hundred cubic centimeters and in the winter between 0.20 and 0.35 mg. The difference was attributed to the lower consumption of fruit during the winter and spring.

Degulf⁷ found a low vitamin C level to be a "normal condition" for the Swedish population during the winter. In 326 healthy persons in the spring, the average vitamin C level was 0.22 mg per hundred cubic centimeters. In the same group in the summer the average was about 0.90 mg. Rietschel⁸ maintained that saturation with vitamin C is not the normal state and opposed the view of Szent-Gyorgyi that an increased intake of vitamin C leads to an "increased general health." He expressed the opinion that scurvy is the only clinical syndrome which has been proved to be due to hypovitaminosis C, and that only small amounts of vitamin C are necessary to prevent that disease.⁹ According to his

4 King, C. G. The Physiology of Vitamin C, *J. A. M. A.* **111** 1098 (Sept 17) 1938.

5 Ingalls, T. H. Studies on the Urinary Excretion and Blood Concentration of Ascorbic Acid in Infantile Scurvy, *J. Pediat.* **10** 577, 1937.

6 Trier, E. Die jahreszeitlichen Schwankungen der Serumascorbinsäure, *Klin. Wchnschr.* **17** 976, 1938.

7 Degulf, H. Zur Frage der C-Hypovitaminose, *Klin. Wchnschr.* **18** 669, 1939.

8 Rietschel, H. C-Vitaminbedarf und C-Hypovitaminose, *Klin. Wchnschr.* **17**-1787, 1938.

9 Rietschel, H. Zur Frage des optimalen und minimalen C-Vitaminbedarfes beim Menschen, *München med. Wchnschr.* **86** 811, 1939.

statements, values of 0.2 and 0.3 mg per hundred cubic centimeters are not abnormal and there is little likelihood of scurvy's developing until the level falls approximately to zero.

Experimental Observations—In our control study, 43 nurses of the Massachusetts General Hospital and 25 students of the Harvard Medical School were selected without regard to dietary habits. All appeared to be in good health. Both groups ate most of their meals in institutions where a balanced diet relatively rich in vitamin C was served. There were some, however, who did not care particularly for fruit. Others enjoyed it a great deal and complemented their daily intake from outside sources. The level of vitamin C in the plasma of the 68 persons (table 1) ranged from 0.10 to 1.46 mg per hundred cubic centimeters. The average was 0.60 mg. The level was below 0.30 mg. in 8 persons. The average for the two groups was essentially the same—0.58 mg. among

TABLE 1—*Experimental Observations on One Hundred and Eighty-One Patients and on Sixty-Eight Apparently Healthy Controls*

| Cutaneous Diseases | Concentration of Vitamin C,
in Mg per 100 Cc of Plasma | | | | |
|-----------------------------------|---|-----------|-----------|-----------|-----------|
| | 0.0-0.14 | 0.15-0.29 | 0.30-0.59 | 0.60-0.99 | Above 1.0 |
| Miscellaneous types of dermatitis | 32 | 13 | 9 | 7 | 2 |
| Psoriasis | 6 | 3 | 11 | 2 | 4 |
| Urticaria | 6 | 3 | 4 | 5 | 1 |
| Lupus vulgaris | 2 | 1 | 4 | | |
| Lupus erythematosus | 2 | 4 | 3 | 4 | 1 |
| Atopic eczema | 4 | 5 | 4 | 6 | 1 |
| Exfoliative dermatitis | 6 | 1 | | 1 | |
| Purpura | 1 | 2 | 1 | | |
| Pemphigus | 6 | | 1 | 1 | |
| Acne vulgaris | 1 | 1 | 5 | 4 | |
| Nurses | 3 | 5 | 15 | 17 | 3 |
| Students | 1 | | 11 | 10 | 3 |

the nurses and 0.62 mg among the students. Most of those with low levels ate fruit only occasionally.

VITAMIN C IN CUTANEOUS DISEASES

Literature—The following reports are believed to be typical of those in the current literature. No attempt has been made to make an exhaustive survey.

(a) *Psoriasis*—Reiss¹⁰ observed a depletion of vitamin C in patients with psoriasis despite an adequate intake. He attributed the depletion to disturbed cellular metabolism of the epidermis and a resultant increased demand for vitamin C. Clinical improvement followed treatment with vitamin C. Lutz¹¹ reported a favorable response to treatment

¹⁰ Reiss, F. Psoriasis vulgaris und Hypovitaminosis C. *Acta dermat* 30:1, 1937.

¹¹ Lutz, W. Einige Beobachtungen über die Beeinflussungsmöglichkeit der Psoriasis durch Ascorbinsäure, *Schweiz med Wchnschr* 65:1169, 1935.

in 3 cases. The lesions, however, recurred subsequently. Volpe¹² noted good results in 5 cases of long-standing psoriasis.

(b) *Urticaria* Rosenberg¹³ determined the vitamin C level of 7 patients with urticaria and found values between 0.31 and 0.52 mg per hundred cubic centimeters. He assumed 0.80 mg to be low normal and suggested that vitamin C deficiency was responsible for the urticaria. Good therapeutic results followed administration of the active substance.

(c) *Lupus Vulgaris* As several observers had reported a deficiency of vitamin C in patients with pulmonary tuberculosis, Wernick¹⁴ determined the excretion of this substance in the urine of patients with lupus vulgaris. In 10 of 14 cases the spontaneous elimination of vitamin C was below 30 mg per day, in 2 cases it was below 50 mg, and in only 2 was it within the normal range, which the author assumed should be above 70 mg per day. An interval longer than that necessary for normal persons was needed to produce with daily administration of 100 mg a significant increase in the amount of vitamin C excreted in the urine. Clinical improvement was not impressive. As an explanation it was noted that the period of administration for each patient was from ten to fifteen days and that possibly this was too brief a period in which to anticipate benefit.

(d) *Lupus Erythematosus* Finkle¹⁵ investigated the urinary elimination of vitamin C in 5 cases of acute lupus erythematosus, and in each instance the amount was low. In studying a large series of patients with various diseases he found that the 5 patients with acute lupus erythematosus were the only ones who did not respond with a steep rise in the urinary elimination of vitamin C after daily administration for one week of 400 cc of orange juice. Favorable therapeutic results were not obtained with ingestion of large quantities of crystalline vitamin C.

(e) *Generalized Exfoliative Dermatitis* Muller¹⁶ reported excellent results following ingestion of vitamin C in 1 case of generalized exfoliative dermatitis of the Wilson-Brocq type.

12 Volpe, I. Ueber mehrere Erfolge in der Psoriasisbehandlung mit Vitamin C, *Schweiz med Wchnschr* **67** 498, 1937.

13 Rosenberg, W. A. Vitamin C Deficiency as a Cause of Urticaria, *Arch Dermat & Syph* **37** 1010 (June) 1938.

14 Wernick, E. Ueber die Ausscheidung der L-Ascorbinsäure (Vitamin C) im Harn, *Dermat Ztschr* **75** 177, 1937, **76** 189, 1937.

15 Finkle, P. Vitamin C Saturation Levels in the Body in Normal Subjects and in Various Pathological Conditions, *J Clin Investigation* **16** 587, 1937.

16 Muller, W. Die Behandlung von Hautkrankheiten mit Vitaminen unter besonderer Berücksichtigung eines Falles von Dermatitis exfoliativa generalisata (Wilson-Brocq), *München med Wchnschr* **83** 2116, 1936.

(f) Eczema In cases of eczema, Araki¹⁷ observed a relatively low excretion of vitamin C after intravenous injection of a constant amount of this substance. Patients used as controls excreted approximately 3 times the quantity that those with eczema did.

(g) Purpura Wolbach¹⁸ expressed the belief that vitamin C is an important factor in the formation of the colloidal intercellular substance of the capillary wall. In scorbutic patients, intake of vitamin C is associated with a return of capillary resistance. Finkle¹⁵ found a normal vitamin C excretion in only 3 out of 19 cases of purpura. Abt and Farmer,³ however, found vitamin C of no avail in the treatment of patients with thrombopenic purpura, and the capillary resistance of the skin remained abnormally low.

Experimental Observations—The 181 patients investigated by us were suffering from various diseases of the skin that are enumerated in table 1. The particular diseases were selected for study because favorable therapeutic effects following a high intake of vitamin C had been reported. The average blood level for this group of patients was 0.36 mg per hundred cubic centimeters. In 55 per cent the level was below 0.30 mg. Throughout the series the values of vitamin C were scattered, in some patients they were high, in others, low. In patients with psoriasis the concentrations varied between 0 and 1.20 mg, with urticaria between 0 and 1.12 mg, with atopic eczema between 0 and 1.13 mg, and with lupus erythematosus between 0 and 1.32 mg. There were 3 diseases, however, in which there appeared to be lower concentrations than in the others. These were purpura, exfoliative dermatitis and pemphigus. Three of 4 patients with purpura, 7 of 8 patients with generalized exfoliative dermatitis and 6 of 8 patients with pemphigus had values below 0.30 mg per hundred cubic centimeters.

A short dietary history was taken of 117 patients. A high intake of vitamin C was assumed if fresh fruit was consumed at least five times each week. A low intake was assumed if fruit was eaten only occasionally. The information obtained from the patients was probably not thoroughly reliable, but was useful as a first approximation. On this basis 40 patients were found to have a high, 30 a moderate and 47 a low intake of vitamin C. The consumption of foods containing vitamin C was considerably lower in the patients than in the controls. This difference was attributed to the lower social strata of the former group. The correlational data of the level of vitamin C in the blood and the intake are given in table 2. There is a high correlation in the extremes

17 Araki, R. Ueber die Ausscheidung von Vitamin C im Harn von verschiedenen Hautkranken, *Jap J Dermat & Urol* 42:132, 1937.

18 Wolbach, S. B. Pathologic Changes Resulting from Vitamin Deficiency, *J A M A* 108:7 (Jan 2) 1937.

Those who usually ate an inadequate diet had low levels in the blood, and those with a good diet had higher levels

TREATMENT WITH VITAMIN C

Eighteen patients with a low level of vitamin C in the blood were given daily over a period of two to ten weeks 200 mg of this substance by mouth. The average level in the blood at the end of this experimental period was 0.97 mg per hundred cubic centimeters.

The numbers of patients and diseases treated were as follows: 5 patients with urticaria, 4 with lupus vulgaris, 3 with eczema, 2 with generalized exfoliative dermatitis, 2 with psoriasis, 1 with purpura and 1 with pemphigus. None of these patients showed improvement which was believed attributable to the high intake of vitamin C.

TABLE 2—*Dietary Intake of Vitamin C and Plasma Levels of One Hundred and Seventeen Patients*

| Dietary Intake of Vitamin C | Concentration of Vitamin C,
in Mg per 100 Cc of Plasma | | | | |
|-----------------------------|---|-----------|-----------|-----------|-----------|
| | 0.0-14 | 0.15-0.20 | 0.30-0.50 | 0.60-0.99 | Above 1.0 |
| Good | 3 | 4 | 16 | 11 | 6 |
| Moderate | 11 | 1 | 9 | 0 | |
| Poor | 26 | 12 | 6 | 1 | 2 |

COMMENT

Normal Persons—Wide variations were observed in the level of vitamin C in apparently healthy persons. In most instances there was a direct correlation between the level of the vitamin in the blood and the consumption of foods which contain it. The average level in the blood was 0.60 mg per hundred cubic centimeters. Only 12 per cent of the group had a concentration less than 0.30 mg, which is believed to be the lower limit of normal.

Persons with Cutaneous Diseases—The average level of vitamin C in the blood of the patients with cutaneous diseases was 0.36 mg per hundred cubic centimeters. A diminished consumption of vitamin C is assumed to be a satisfactory explanation. It is believed that the level of vitamin C in the blood bears no relation to the development of psoriasis, urticaria, lupus erythematosus, lupus vulgaris, acne and dermatitis. On the other hand, the number of patients with purpura, pemphigus and generalized exfoliative dermatitis who had low blood vitamin C values may be significant. The fact that high values can occur in these diseases militates, however, against any etiologic connections. Further, one should keep in mind that in addition to having a low intake of vitamin C the majority of these patients were ill and had fever, and in severe illnesses, such as pneumonia, diphtheria and tuber-

culosis, a diminished concentration of vitamin C has been reported. Degulf⁷ observed the following values in 255 patients with tuberculosis. In the spring the average was 0.10 mg per hundred cubic centimeters (controls, 0.22 mg), while in the summer the average was 0.47 mg (controls, 0.90 mg). Trier⁸ made similar observations on patients with acute febrile or pyogenic diseases. He noticed that patients who came into the hospital with a sudden febrile disease and a normal vitamin C level showed a gradual decrease of this substance in the blood. He concluded that under such circumstances the body uses more vitamin C than otherwise.

The higher average vitamin C level in the group of normal persons (0.60 mg per hundred cubic centimeters) than in the group of patients (0.36 mg) can probably be explained by the diet. The diet of most of the normal persons was thought to be adequate in vitamin C. If comparison is made between the normal persons and the patients with a similar adequate intake, the results are similar. That is, 87 per cent of the normal persons and 82 per cent of the patients on an adequate diet had blood concentrations greater than 0.30 mg.

SUMMARY

The literature on the role of vitamin C in cutaneous diseases is reviewed. The vitamin C content was determined in the blood of 68 apparently healthy persons and of 181 patients with various diseases of the skin. Eighteen of these patients received treatment with large amounts of vitamin C.

CONCLUSIONS

1 The level of vitamin C in the blood bears a direct relation to the intake of foods which contain this substance.

2 Apparent good health may be maintained with a low concentration of vitamin C in the body.

3 There is no direct correlation between the level of vitamin C in the blood and the development of the several diseases of the skin which were investigated.

4 Most patients with pemphigus, purpura or generalized exfoliative dermatitis had low levels of vitamin C in the blood. The probable explanation is that most of these patients had been ill for a long period with an elevated temperature. The patients with other cutaneous diseases investigated had wide scattering of values.

5 Eighteen patients with various diseases of the skin under treatment with large amounts of vitamin C showed no coincidental improvement.

Dr C. Guy Lane assisted in the preparation of this paper.

TREATMENT OF PSORIASIS WITH CONCENTRATED VIOSTEROL

UNDER THE AUSPICES OF THE CINCINNATI SOCIETY
OF DERMATOLOGY AND SYPHILOLOGY

GEORGE E CLARKE, MD
CINCINNATI

Because of the involution of many psoriatic lesions during the summer months, when there is the greatest exposure to sunlight, Krafka¹ was led to the hypothesis that large quantities of vitamin D would be beneficial in the treatment of psoriasis. Three patients were treated with halibut liver oil with viosterol or with viosterol in varying amounts up to 20,000 U S P units of vitamin D per day. In 2 cases the condition was of long standing, in the other, of fairly recent origin. In all there was material improvement.

Cedar and Zon² reported the treatment of 15 patients with irradiated ergosterol. Doses ranged from 300,000 to 400,000 U S P units of vitamin D per day. Of the 15 patients treated, 11 showed complete involution in from six to twelve weeks. Recurrence occurred in 6 patients in six weeks to five months after discontinuance of the treatment.

Reactions to and toxic effects of massive doses of vitamin D have been discussed by many authors and were reviewed by Tauber and Clarke³.

In the fall of 1937 members of the Cincinnati Society of Dermatology and Syphilology were given the opportunity to determine the value of massive doses of vitamin D in psoriasis.

Material of two kinds was used. One was natural fish oil adjusted so that each capsule contained 50,000 U S P units of vitamin D and not more than 50,000 U S P units of vitamin A. The other consisted of a concentrated selectively irradiated ergosterol in oil (viosterol in

1 Krafka, J. A Single Treatment for Psoriasis, *J Lab & Clin Med* **21** 1147-1148, 1936

2 Cedar, E T, and Zon, L. Treatment of Psoriasis with Massive Doses of Crystalline Vitamin D and Irradiated Ergosterol, *Pub Health Rep* **52** 1580-1584, 1937

3 Tauber, E B, and Clarke, G E. Treatment of Pemphigus with Concentrated Viosterol, *Arch Dermat & Syph* **40** 82-89 (July) 1939

oil), each capsule containing 50,000 U S P units of vitamin D.⁴ One group of members was given the natural oil, and another group, the viosterol in oil

Thirty-seven patients with psoriasis were treated with the natural fish oil, while 107 were treated with the viosterol in oil. The accompanying table gives the results of the experiment

| Source of Vitamin D | Number of Patients | Average Dose in U S P Units | Average Length of Treatment | Complete Relief | Slight Improvement | No Improvement | Reactions |
|---|--------------------|-----------------------------|-----------------------------|-----------------|--------------------|----------------|-----------|
| Natural fish oil | 37 | 300,000 to 400,000 | 3 to 4 months | None | 30% | 70% | Mild |
| Viosterol in oil (irradiated ergosterol in oil) | 107 | 300,000 to 400,000 | 3 to 4 months | 12% | 15% | 73% | Mild |

COMMENT

Of the 37 patients treated with the natural fish oil, none showed complete involution of psoriatic lesions, while only 30 per cent showed any improvement. Not only did the remaining 70 per cent show no improvement, but some of them even became worse under treatment. Of the 107 patients treated with viosterol in oil, 12 per cent showed complete involution, 15 per cent slight improvement and 73 per cent no change.

All the patients were treated during the winter months, so that climatic conditions would not influence the results. Adjunctive treatment was used in only a few cases, but did not seem to influence the results in any way. The adjunctive treatment consisted only of local applications of petrolatum, hydrous wool fat and small doses of ultraviolet radiation. Roentgen ray treatment was given to selected areas in a few cases, but the control areas in these cases were not affected by massive doses of vitamin D.

SUMMARY

Natural fish oil in massive doses, yielding 300,000 to 400,000 U S P. units of vitamin D, was given to 37 patients with psoriasis daily for periods of three to four months.

Viosterol in oil (irradiated ergosterol in oil) in similar massive doses, of 300,000 to 400,000 units of vitamin D, was given to 107 patients with psoriasis daily for periods of three to four months.

Only 12 per cent of the patients receiving viosterol in oil showed complete involution of psoriatic lesions.

Seventy per cent of both groups showed no improvement under this type of therapy.

⁴ Both types of capsules were furnished by the Wm S Merrell Company, Cincinnati.

CONCLUSIONS

- 1 Both natural and synthetic vitamin D preparations are safe to give in massive doses over long periods of time
- 2 This type of therapy is unreliable to control or to cause involution of psoriatic lesions

RATE OF ULCERATION OF EPITHELIOMAS OF THE SKIN AND LIP

WILLIAM D WILSON, M D

SAVANNAH, GA

Since Broders¹ made known his application of natural laws to evolve the principle of grading carcinomas as to their degree of malignancy, this basis for determining the prognosis and the proper treatment for cancer has become more and more essential to the armamentarium of the pathologist, the surgeon and the roentgenologist. Numerous reports² may be found in the literature concerning its dependability both in determining the prospect for cure and as a guide to the type of treatment which may be most beneficial for a particular condition. The bulk of this work, however, is concerned with the future of the patient rather than with the evolution of the growth itself. Broders^{1a, b} noted a close association of the size of the epitheliomas of the skin and lip and their grade of malignancy, but I have not observed in the literature any attempt to correlate these factors with the duration of the lesion.

Obviously lesions of the skin and lip lend themselves most readily to this type of study, because, although admittedly it is difficult and

Abridgment of a thesis submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Surgery. When this work was done the author was a Fellow in Surgery at the Mayo Foundation.

1 Broders, A. C. (a) Squamous-Cell Epithelioma of the Lip. A Study of Five Hundred and Thirty-Seven Cases, *J. A. M. A.* **74**:656-664 (March 6) 1920, (b) Squamous-Cell Epithelioma of the Skin. A Study of Two Hundred and Fifty-Six Cases, *Ann. Surg.* **73**:141-160 (Feb.) 1921, (c) Epithelioma of the Genito-Urinary Organs, *ibid.* **75**:574-604 (May) 1922, (d) Epithelioma of Cavities and Internal Organs of the Head and Neck, *Arch. Surg.* **11**:43-73 (July) 1925.

2 Broders, A. C. The Grading of Cancer. Its Relationship to Metastasis and Prognosis, *Texas State J. Med.* **29**:520-525 (Dec.) 1933. Dufourmentel, L. Le traitement curatif du cancer de l'oesophage, *Paris méd.* **2**:87, 1930, abstracted, *Am. J. Cancer* **15**:1746 (July) 1931. Greenough, R. B. Varying Degrees of Malignancy in Cancer of the Breast, *J. Cancer Research* **9**:453-463 (Dec.) 1925. Harrington, S. W. Carcinoma of the Breast. Surgical Treatment, and Results Five, Ten, and Fifteen Years After Radical Amputation, *Surg., Gynec. & Obst.* **56**:438-441 (Feb.) 1933. Karsner, H. T., and Clark, B. Analysis of One Hundred and Four Cases of Carcinoma of the Large Intestine, *Am. J. Cancer* **16**:933-970 (Sept.) 1932. Lindberg, L. Fundamental Principles in the Grading of Malignancy of Tumors, *Southwestern Med.* **19**:413-421 (Dec.) 1935. Stewart, F. W., and Spies, J. W. Biopsy Histology in the Grading of Rectal Carcinoma, *Am. J. Path.* **5**:109-115 (March) 1929.

often impossible to obtain precise information as to the time of onset of an epithelioma, the data concerning the duration of a lesion are more nearly correct when the growth is obvious to the patient than when hidden in an organ such as the stomach or colon. Basal cell epitheliomas are also included in this study,³ because they apparently arise from the same layer as the squamous cell types and because of the difficulty sometimes encountered clinically in distinguishing them from the squamous cell types. It was hoped at the outset of this study that some criteria might possibly be found on which an approximation of the grade of malignancy could be based if the duration of the lesion were known.

MATERIAL AND METHOD

The records of 3,221 cases of epithelioma of the skin and lip were perused in order to obtain the material for this study. Of this number 793 cases of squamous cell epithelioma had been used previously by Broders^{1a, b} as a partial basis for the grading of cancer, and 268 cases of basal cell epithelioma had been reported by him.¹ From this material data were obtained concerning the age of the patient, the type, grade, duration and site of the epithelioma and the nature of previous treatment, if any. Special attention was paid to whether or not the patient had been treated with an arsenical preparation, roentgen rays or radium. Only cases in which ulceration was present were used. The area of the ulcers was used as a basis for most of the figures presented. In many instances an accurate measurement had been taken by the pathologist and was available. Clinical approximations of size were not accepted. The gross pathologic material was studied, and the ulcer was measured in instances in which an accurate measurement had not been recorded. Cases were excluded in which neither a previous measurement nor enough pathologic material to obtain an accurate measurement was available. Also excluded were cases in which a definite statement in the history concerning the exact or approximate date of onset of the epithelioma had not been made. Thus 1,265 cases were used in this study.

This total was made up of 28 (2.2 per cent) cases of squamous cell epithelioma of grade 4 (on the basis of 1 to 4), 161 (12.7 per cent) cases of squamous cell epithelioma of grade 3, 425 (33.5 per cent) cases of squamous cell epithelioma of grade 2, 144 (11.4 per cent) cases of

3 (a) Owen, M. Basal Cell Carcinoma. Study of Eight Hundred and Thirty-Six Cases, *Arch Path* **10** 386-394 (Sept) 1930. (b) Ewing, J. Neoplastic Diseases. A Treatise on Tumors, Philadelphia, W. B. Saunders Company, 1922, p. 474. (c) Montgomery, H. Histogenesis of Basal-Cell Epithelioma, *Radiology* **25** 8-23 (July) 1935.

4 Broders, A. C. Basal-Cell Epithelioma, *J. A. M. A.* **72** 856-860 (March 22) 1919.

squamous cell epithelioma of grade 1, and 410 (32.4 per cent) cases of basal cell epithelioma. Also there were 97 (7.8 per cent) cases of what Montgomery⁵ called basal-squamous cell epithelioma. If the cases of epitheliomas of the lip are excluded, this group comprises 10.4 per cent of the cases of cutaneous epithelioma. This figure corresponds rather closely to Montgomery's statement that approximately 12 per cent of epitheliomas are of the basal-squamous cell type. Of the basal-squamous cell epitheliomas, 84 (6.6 per cent) were of combination basal cell and squamous cell epithelioma of grade 1, and 13 (1.2 per cent) were of basal cell and squamous cell epithelioma of grade 2.

To compute the area of circular ulcerated epitheliomas the formula πr^2 was used. The area of oval lesions was computed by use of the formula πab , in which a and b equal the greater and lesser radii of the oval, respectively. The epitheliomas were classified on the basis of their grade of malignancy and were compared as to previous treatment or neglect of treatment. The treated epitheliomas also were studied as to the type of treatment previously employed. The site of the lesions was considered, as was the age of the patient. Although the group of cases in which previously given arsenicals and irradiation were causative factors in the formation of the epithelioma was small, it also was considered separately. For the sake of comparison, the average of the areas of the ulcers for each year for each group and the various grades of malignancy were made into composite graphs. For brevity in the charts squamous cell epithelioma is abbreviated S C E, basal cell epithelioma is shown as B C E, and basal-squamous cell epithelioma is shown as B S C E. For the squamous cell epitheliomas, the grade of malignancy is denoted by the numeral that follows the identifying letters.

TREATED AND UNTREATED EPITHELIOMAS

The available material was divided into the cases of patients who had not received treatment previous to registration at the clinic and the cases of those who had been treated previously. Patients who previously had used various pastes and ointments were relegated to the "treated" group. As is shown in the charts, the average area of ulceration of squamous cell epitheliomas increases in direct proportion to the grade of malignancy except with squamous cell epithelioma of grade 4. In chart 1 the data on tumors of grade 4, were not graphed because of the few cases obtainable. In chart 2 the average area of grade 4 squamous cell epitheliomas is shown to lie between that of grade 1 and that of grade 2. A possible explanation is that with tumors of this type extension occurred deeply into the tissue rather than laterally. It has been

⁵ Montgomery, H. Basal Cell Epithelioma, *Arch. Dermat. & Syph.* 18:50-73 (July) 1928.

shown that in this group of patients with squamous cell epithelioma metastasis occurred earlier than it did in those with growths of lower grades of malignancy and that the prognosis was uniformly poorer than in those with lower grades of malignancy^{1a, b}

Further comparison of the charts shows that in the treated group the average area of ulceration was uniformly larger than in the group

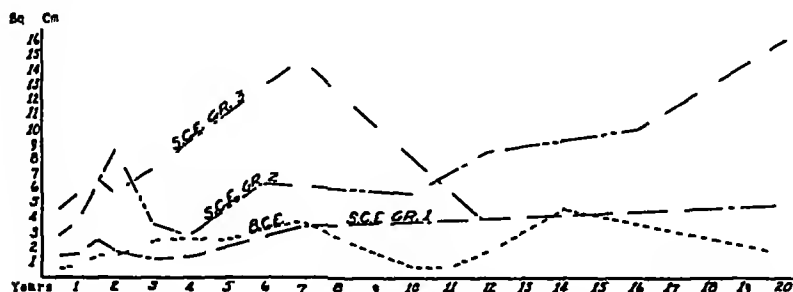


Chart 1—The relation of the size of untreated epitheliomas to the duration of the lesions The abbreviations are explained in the text

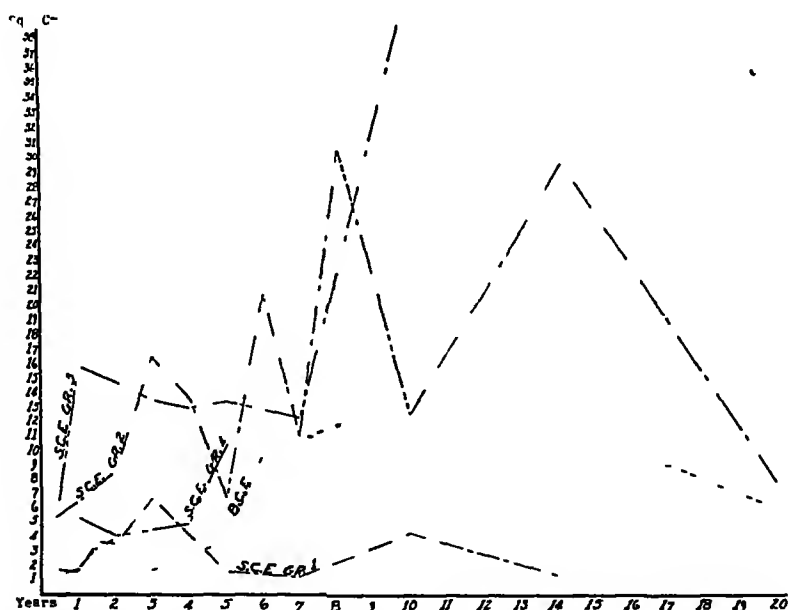


Chart 2—The relation of the size of treated epitheliomas to the duration of the lesions The abbreviations are explained in the text

who had not received previous treatment This is understandable and is to be expected, because the treated group considered here is comprised of patients in whom the results of treatment were poor, the attempted treatment apparently acted as a stimulus to growth rather than as a curative measure

The basal cell epitheliomas apparently had approximately the same area as the squamous cell epitheliomas of grade 1 However, in the

treated patients whose epitheliomas were of longer duration there was an increase in size over that of the squamous cell epitheliomas of grade 1

For the patients in whom lesions had recurred many forms of therapy had been employed previously. Among these were excision, cautery, irradiation, diathermy and application of escharotics, solid carbon dioxide, peruvian balsam, phenol, paste of zinc oxide, silver nitrate, iodine, ultraviolet rays and various salves, ointments and pastes the ingredients of which are unknown.

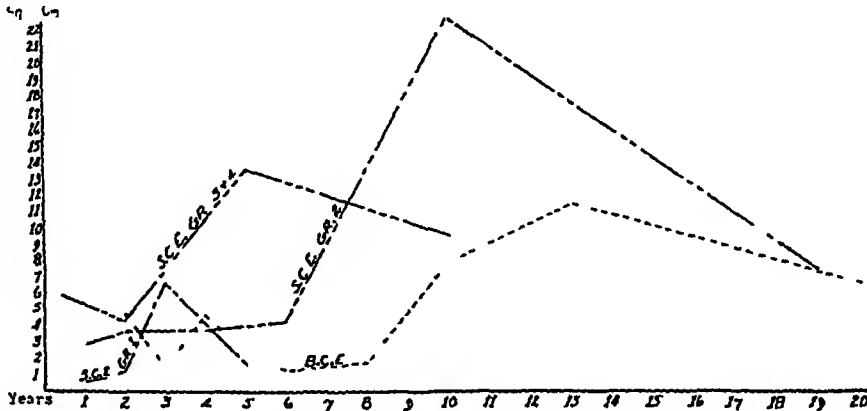


Chart 3—The relation of the size of the epitheliomas treated previously with irradiation to the duration of the lesions. The abbreviations are explained in the text.

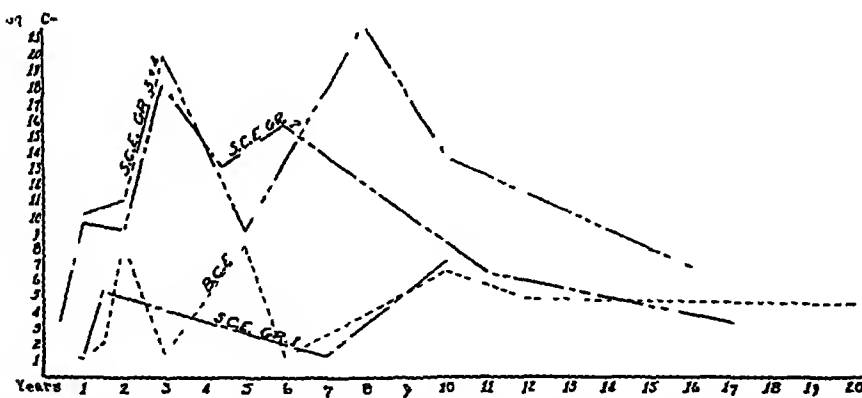


Chart 4—The relation of the size of the epitheliomas treated previously with excision and diathermy to the duration of the lesions. The abbreviations are explained in the text.

For convenience in study the patients were placed in three groups: those previously treated by irradiation, those treated by excision and diathermy, and those whose only treatment had been by salves and ointments. Charts 3, 4, and 5 show a comparative study of the areas of the lesions according to grade for each type of treatment. In these charts squamous cell epitheliomas of grades 3 and 4 are combined because in both grades differentiation of cells was not great and the number of grade

4 epitheliomas was too small to give an accurate graph. The higher grades of epithelioma showed recurrences of smaller size when previously treated by irradiation than when treated by either of the other two methods. Squamous cell epithelioma of grade 2 showed approximately the same size on recurrence when treated with irradiation as when treated by excision and diathermy. However, a rapid rate of ulceration was noted when escharotics or salves were used (chart 5). There seemed to be little influence on squamous cell epithelioma of grade 1 with any type of treatment. Basal cell epithelioma also, except for a discrepant peak, shown in chart 5, was comparatively little influenced

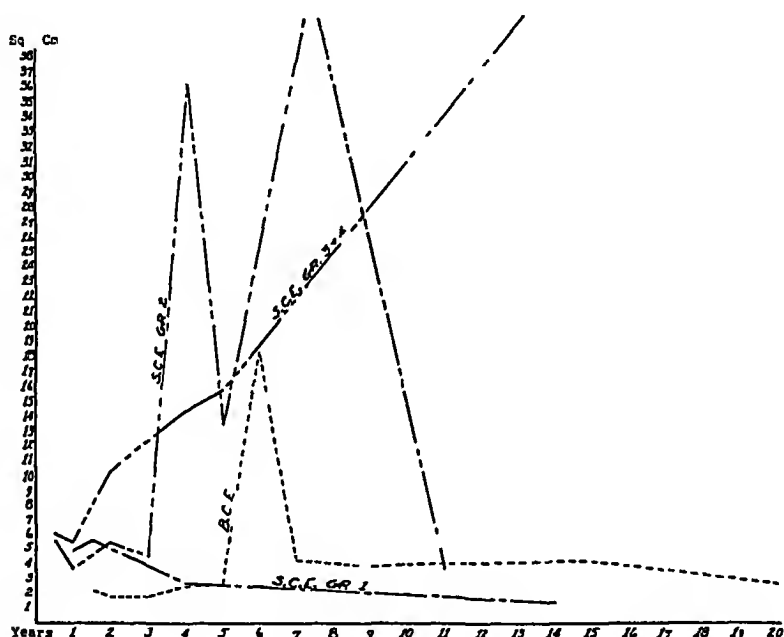


Chart 5—The relation of the size of the epitheliomas treated previously with salves, ointments and pastes to the duration of the lesions. The abbreviations are explained in the text.

Particularly notable also was the response of squamous cell epithelioma of grades 3 and 4 to abuse of treatment with salves and pastes. Its growth was unabated, rapid and fulminating. In spite of this, Valade,⁶ who gave an excellent historical review of the use of arsenic paste in the treatment of ulcers and epitheliomas through the ages, stated that many reputable dermatologists continue to use it in the treatment of epithelioma of the skin.

⁶ Valade, C. K. Arsenic Paste in Cancer of the Skin, *J. Michigan M. Soc.* 33: 513-516 (Sept.) 1934.

THE SITES OF EPITHELIOMA

It is agreed⁷ generally that epithelioma, particularly basal cell epithelioma, is more frequently found about the head than elsewhere on the body. Broders⁸ observed that 78.04 per cent of the squamous cell epitheliomas of the skin and 96.28 per cent of the basal cell epitheliomas were situated above the clavicle. The various lesions situated above the clavicle in this series are: squamous cell epithelioma of grade 4, 78.6 per cent, squamous cell epithelioma of grade 3, 85.7 per cent, squamous cell epithelioma of grade 2, 86.6 per cent; squamous cell epithelioma of grade 1, 79.9 per cent, and basal cell epithelioma, 97.4 per cent. Of the group of basal-squamous cell epitheliomas, 97.7 per cent were situated

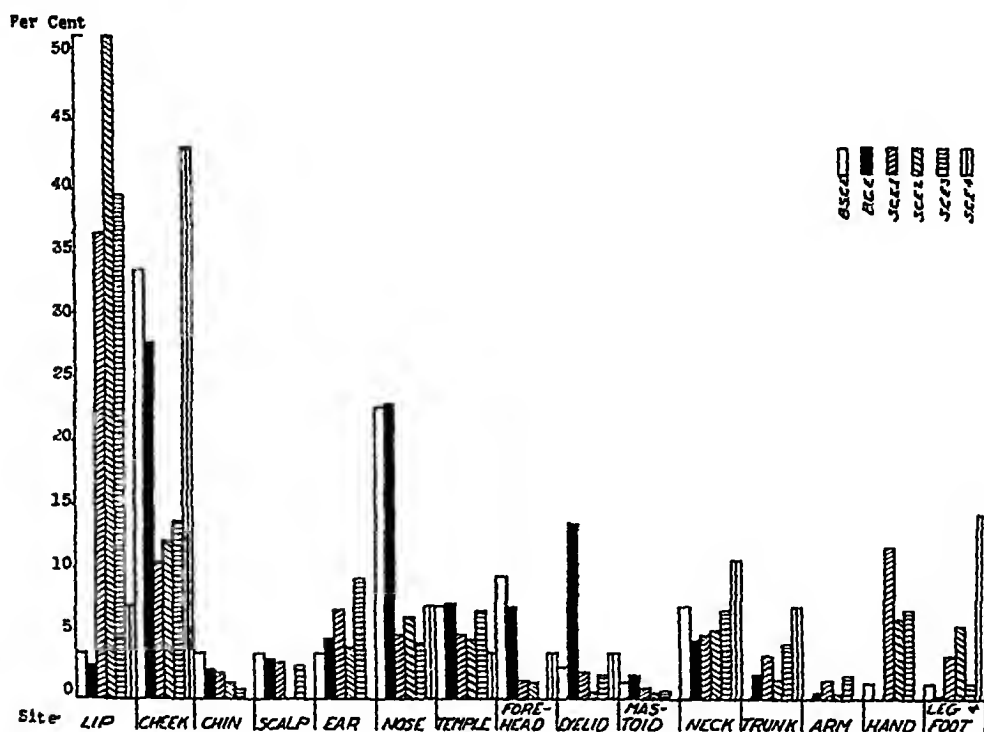


Chart 6—The percentage distribution of the epitheliomas according to the site of the lesions. The abbreviations are explained in the text.

above the clavicle. Chart 6 shows these figures in a more complete form. The percentage of the total number of epitheliomas in each group is shown in relation to the site of the lesion.

⁷ Schreiner, B. F. Squamous-Cell Carcinoma of the Skin, *Am J Cancer* 19:829-837 (Dec) 1933. Howles, J. K. Epithelioma of the Skin and Oral Mucous Membranes, *South M J* 28:494-503 (June) 1935. Warren, S., Gates, O., and Butterfield, P. W. The Value of Histologic Differentiation of Basal Cell Carcinoma, *New England J Med* 215:1060-1064 (Dec) 1936. Walker, N. An Introduction to Dermatology, New York, William Wood & Company, 1925, p. 324. Zeisler, E. P. Cancer of the Skin, *Surg, Gynec & Obst* 56:472-475 (Feb) 1933. Montgomery^{3c} Owen³¹.

⁸ Broders, footnotes 1a and 4.

THE FACTOR OF AGE

Although it is admitted that senile changes in the skin are dependent on such factors as exposure, heritage and occupation and that senile changes occasionally begin early in life,⁹ an age of 56 was selected empirically as the dividing line in a study of the comparative size of ulcers in relation to the various grades of malignancy. By the selection of this age the groups were of approximately the same size. The observations in this study are noted in charts 7 and 8. In the groups of patients with basal cell epithelioma and squamous cell epithelioma of grade 1, there is little difference in the size of ulcerated areas in the two age groups. There is a tendency for the lesions in the old patients to be larger than those in the young patients. Squamous cell epitheliomas of grades 2 and 3 were considerably larger in the older age group than in the younger. A possible explanation lies in the loss of elasticity of the skin with increasing age.⁹

EPITHELIOMA AND ARSENICAL PREPARATIONS

Paris¹⁰ (1820) is credited with being the first to note the carcinogenic property of arsenic. Hutchinson¹¹ first suggested the etiologic relation between the clinical use of arsenic in treatment and carcinoma of the skin when he reported 5 cases in which cancer of the skin had occurred after the use of arsenic in the treatment of psoriasis and a sixth case in which arsenic was used in the treatment of pemphigus. Montgomery¹² stated that inorganic pentavalent, and occasionally even trivalent, arsenic may have an affinity for the epidermis. Solution of potassium arsenite had been administered previously to the majority of Montgomery's patients. He stated that the lesions sometimes appeared as late as thirty years after the ingestion of the drug and that neither the amount of arsenic nor the length of time over which it was taken seemed to have any bearing on the result among patients who had keratosis due to arsenic. Epitheliomas developed in 20 per cent of his patients, either in the keratotic lesions or as superficial epitheliomas elsewhere on the body.

9 Sutton, R. L. *Diseases of the Skin*, ed 8, St. Louis, C. V. Mosby Company, 1931, p. 571.

10 Paris, quoted by Franseen, C. C., and Taylor, G. W. *Arsenical Keratoses and Carcinomas*, *Am. J. Cancer* 22: 287-307 (Oct.) 1934.

11 Hutchinson, J. *On Some Examples of Arsenic-Keratosis of the Skin and of Arsenic-Cancer*, *Tr. Path. Soc., London* 39: 352-363, 1888.

12 Montgomery, H. *Arsenic as an Etiologic Agent in Certain Types of Epithelioma. Differential Diagnosis from, and Further Studies Regarding, Superficial Epitheliomatosis and Bowen's Disease*, *Arch. Dermat. & Syph.* 32: 218-236 (Aug.) 1935.

In 9 cases of this series the lesion was diagnosed as being arsenical in origin. There were 1 case of basal cell epithelioma, 3 of squamous cell epithelioma of grade 1 and 5 of squamous cell epithelioma of grade 2. In 5 cases the area of the ulcer was larger than the average

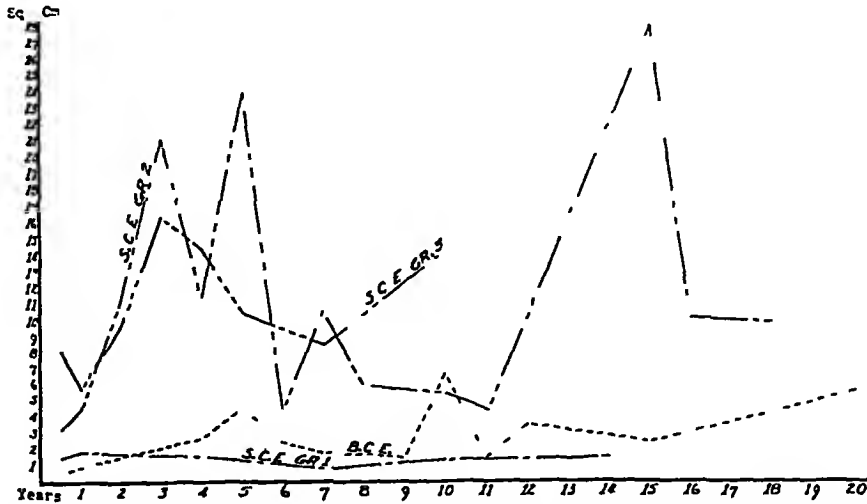


Chart 7—The relation of the size of the epitheliomas to the duration of lesions in patients less than 56 years old. The abbreviations are explained in the text.

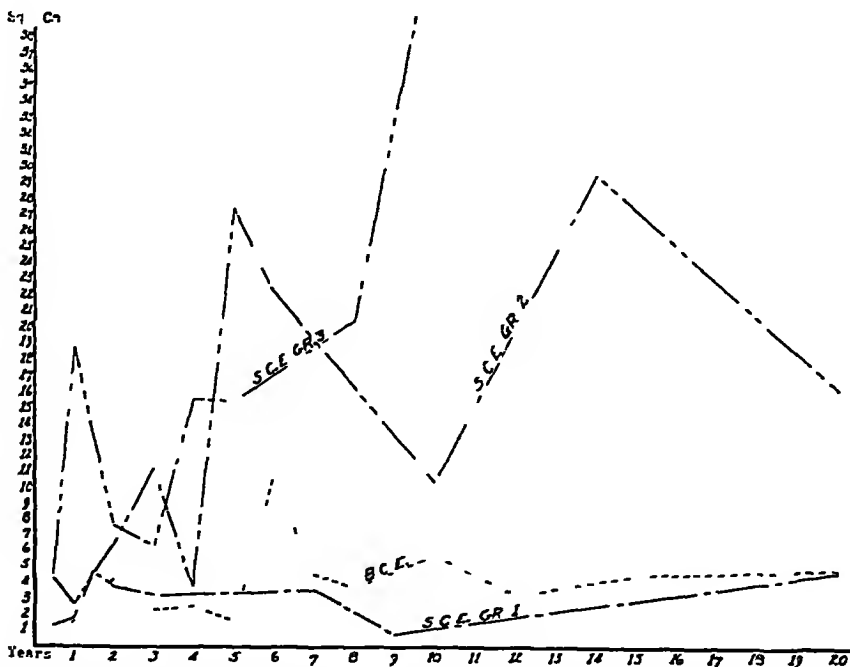


Chart 8—The relation of the size of the epitheliomas to the duration of the lesions in patients more than 56 years old. The abbreviations are explained in the text.

of the corresponding untreated lesions, and in 4 cases the lesions were smaller than the average of the corresponding untreated group. In regard to location, the lesions were observed on all parts of the body,

4 on the hand, 3 on the forehead, 1 on the neck and 1 in the groin. The age of the patients, with an average of 50.7 years, was found to be of no significance.

EPITHELIOMAS AND IRRADIATION

Cole¹³ gave an excellent historical review of roentgen ray dermatoses and their relation to the development of carcinoma of the skin. He described the microscopic picture of roentgen ray dermatosis as a chronic degenerative change resulting from sclerosis of the vessels supplying the skin. The glandular elements of the dermis are said to disappear, and the dermis is much thickened from the formation of a degenerated hyaline, collagen-like material. Telangiectases appear as newly formed capillaries and attempt to reestablish the lost blood supply of the dermis. He agreed with Wolbach¹⁴ that the changes which occur in the epidermis are secondary to destructive changes in the supporting layer. Both authors stated the belief that the acquisition of malignant properties follows sustained proliferative activities in contact with abnormal connective tissue.

Twenty-two patients of this series had a history of a burn sustained previously and caused by irradiation of the area on which the epithelioma later appeared. Of this group 1 patient had basal cell epithelioma, 10 had squamous cell epithelioma of grade 1, 4 had squamous cell epithelioma of grade 2, 5 had squamous cell epithelioma of grade 3 and 2 had squamous cell epithelioma of grade 4. As would be expected, the hand was the most common site of the lesions. In the series, 7 lesions were found on the hand, 4 on the trunk, 3 on the nose, 3 on the neck and 1 each on the temple, cheek, chin and arm. Sixteen of these lesions were larger than the average untreated epithelioma of the corresponding group, and 6 were smaller. The average age at which the epitheliomas occurred was 49.6 years.

SUMMARY

An attempt has been made to correlate the rate of ulceration in 1,265 cases of epithelioma of the skin and lip with factors such as the grade of malignancy of the lesion, the type of previous treatment, if any, the site of the lesion and the age of the patient.

In the cases of squamous cell epithelioma, the rate of ulceration was found to be directly proportional to the grade of malignancy except

13 Cole, H. N. Chronic Roentgen-Ray Dermatoses as Seen in the Professional Man, *J. A. M. A.* **84**: 865-874 (March 21) 1925.

14 Wolbach, S. B. A Summary of the Effects of Repeated Roentgen-Ray Exposures upon the Human Skin, Antecedent to the Formation of Carcinoma, *Am. J. Roentgenol.* **13**: 139-143 (Feb.) 1925.

with the lesions of grade 4, which were found to ulcerate at a rate between that of grade 1 and that of grade 2

Previously treated epitheliomas were found to ulcerate more rapidly than those which had not been treated

In the cases of recurrent epithelioma, the rate of ulceration was found to be most rapid in the growths previously treated with salves and pastes

In general, the rate of ulceration was found to be more rapid in persons more than 56 years of age than in the younger persons

That the curves representing the rates of ulceration of the epitheliomas are not smooth may be explained by the facts that the various groups were of small size and that there is no sharp line of distinction between the various grades of malignancy but a gradually increasing dedifferentiation as the grade of malignancy increases

MULTIPLE SYMMETRIC GANGRENE OCCURRING DURING PROLONGED ADMINISTRATION OF AMINOPYRINE

REPORT OF A CASE

J ARTHUR BUCHANAN, M D

BROOKLYN

In most instances the origin of symmetrical gangrene is impossible to explain. I wish to report the following case as the cause seems reasonably clear and the degree of involvement was extensive.

REPORT OF CASE

D M, an unmarried woman aged 32, an underwear operator, was first seen by me on June 1, 1936. Her father and mother, three brothers and one sister were all living and well. The menstrual history was normal, and the only previous illness was measles in childhood. The patient drank coffee and wine rarely. The original consultation was to seek relief from articular disturbance associated with generalized weakness, both of which began four years previously when the right wrist began to be painful and later to swell. The weakness and lack of endurance had been slowly progressive, and after a year of debility pain developed in the feet, and the right knee joint became painful and swollen. During the second year of illness all the joints of both hands became swollen and painful. The hands could not be closed. The left elbow had become involved in recent months. There were no paresthesias in the hands or feet. The appetite had been poor for years, and the capacity of the stomach was small. The bowel evacuations were normal.

The articular disturbance had been diagnosed by "a joint specialist" as the expression of diffuse phlebitis, and the patient had received "special medicine" by hypodermic injection.

At the time of my first examination of the patient her height was 59½ inches (151.13 cm) and her weight 87 pounds (39.5 Kg), representing a loss of 18 pounds (8.2 Kg) in four years. The blood pressure was 110 systolic and 70 diastolic. The right wrist, the left elbow and the second joint of all fingers were swollen, and there was effusion into the left knee joint. In the left elbow the extension was 15 degrees less than complete. The reflexes were all present. The tonsils were small. The tongue was red and slightly fissured. The muscles of the right forearm were atrophic. There was slight recession of the gums.

The hemogram was normal. The Wassermann reaction of the blood was negative. The urine showed a faint trace of albumin and an occasional finely granular cast. The sedimentation readings were 10, 18, 24 and 30 mm in four fifteen minute periods.

The patient was given a high vitamin diet and the general routine for nonspecific arthritis.

She improved slowly and on Dec 26, 1936 resumed her usual occupation, although she still had some swelling at the metacarpophalangeal joints, the right

wrist and the right ankle. Her weight had increased 10 pounds (4.5 Kg). In the latter part of February 1937 she began to have more pains in the joints and some increased swelling in the knee joints. On March 6, 1937 she was given 5 grains (0.32 Gm) of aminopyrine four times a day and 50 mg of ascorbic acid in tablets three times a day after meals. The hemoglobin concentration was 75 per cent (Sahli and Dare), the red blood cell count 3,680,000 and the white blood cell count 8,720 with a normal differential count. She discontinued working on April 24, 1937. The joints were all greatly improved. There was slight edema of both legs. On May 15, 1937 the improvement had continued but the edema of both legs had persisted and there was tenderness throughout the swollen area.

On May 27, 1937 the legs suddenly became greatly swollen from the knees to the ankles, and toward the end of the day bluish spots appeared on the thighs after a period of pain. On May 28 large bluish areas appeared on the backs of both arms and on the forearms, but they were not painful. Nausea was also present. She was seen on May 29 and stated that her condition had become



Distribution of lesions on lower extremities

worse in the last twenty-four hours. There was a painful bluish area at the top of the left ear and also one on the back of each arm, another on each nipple area and one on the back of the buttocks on each side, extending to the ankle. The swelling had disappeared from all the joints. The weight had increased to 101½ pounds (46.05 Kg). The hemoglobin content was 65 per cent, the platelet count 130,000, the red blood cell count 3,280,000 and the white blood cell count 5,300, with polymorphonuclear leukocytes 70 per cent, endotheliocytes 2 per cent and lymphocytes 28 per cent. The urine showed a trace of albumin and contained 8 mg of ascorbic acid per hundred cubic centimeters of urine.

All medication was discontinued, and she was admitted on May 31, 1937 to Wyckoff Heights Hospital.

The color of the lesions steadily changed from blue to black and at the same time became very hard. The pain in the lesions was intense. The patient's mind was clear, and she was cooperative. The appetite was good, the bowels moved regularly. The temperature was 103 F on admission and remained at that level until two days before death, when it fell to 98.5 F, the temperature remained at that level for nearly twenty-four hours, after which it rose to 102.3 F and remained there until June 22, 1937, when the patient died.

On June 1, 1937 the hemoglobin content was 78 per cent, the red blood cell count 3,490,000 and the white blood cell count 13,800. The urine was normal. On June 4 the urine gave a 1 plus reaction for albumin. On June 6 a friction rub was audible anteriorly over the lower lobe of the left lung. On June 7 the hemoglobin content was 57 per cent, the red blood cell count 2,150,000 and the white blood cell count 17,600.

On June 10 the necrotic areas were loosening at the edges. On June 14 the pain in the necrotic areas was intense. The necrotic tissue was removed over the buttocks and legs. The entire skin and subcutaneous tissues were removed, the muscles being left exposed. There was no hemorrhage. On June 18 the general condition was becoming worse, and the hemoglobin content was 50 per cent, the red blood cell count 2,050,000 and the white blood cell count 19,500. The differential counts were always normal. A transfusion of 500 cc of whole blood was given.

On June 22 the patient suddenly began to vomit. The breathing became rapid, the pulse increased in rate, and she died suddenly.

SUMMARY

A case of bilateral symmetric gangrene in a patient with chronic nonspecific arthritis is reported. The gangrene occurred during the prolonged administration of aminopyrine.

RELAPSING FEBRILE NONSUPPURATIVE PANNICULITIS

REPORT OF TWO CASES

I L TILDEN, M D

H C GOTSHALK, M D

AND

E V AVAKIAN, M D

HONOLULU, TERRITORY OF HAWAII

In recent years a number of reports have appeared in the literature of an interesting clinicopathologic syndrome known as relapsing febrile nonsuppurative panniculitis. The condition is characterized by recurrent attacks of subcutaneous nodules, accompanied in most cases by fever and presenting a definite histologic picture. Essentially there are a phagocytosis of the subcutaneous fat, inflammatory cellular infiltration and later healing, often with depression of the overlying skin. The etiology is obscure, although most writers on the subject have found a rather high incidence of focal infection. Previous ingestion of iodides and bromides has been observed in a number of cases.

According to Bailey,¹ who added 5 cases to the literature in 1937, the syndrome was described first by Pfeifer in 1892 and then by Gilchrist and Ketron in 1916 and Weber in 1925. He summarized additional cases reported by Christian, Alderson and Way, Netherton, Weber and Brill, which, with his 5 cases, brought the total number reported to 13.

Since that time an additional 5 cases have appeared in the literature. Reed and Anderson² described a case in 1937 which falls definitely into this group. The patient was a 34 year old woman with subcutaneous nodules distributed in crops over the lower extremities and abdomen, accompanied by fever. She had been on a vitamin-poor diet, and the lesions disappeared when she was given an adequate diet. Cummins and Lever³ in September 1938 added reports of 2 more cases.

From the Departments of Pathology and Internal Medicine, Queen's Hospital

1 Bailey, R J. Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), *J A M A* 109 1419 (Oct 30) 1937

2 Reed, A C, and Anderson, H H. Relapsing Nonsuppurative Panniculitis, *California & West Med* 47 325 (Nov) 1937

3 Cummins, L J, and Lever, W F. Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), *Arch Dermat & Syph* 38: 415 (Sept) 1938

to the literature, both the patients were 10 year old girls with lesions confined to the lower extremities. The histologic description of the lesions is excellent. Shaffer⁴ in October 1938 reported a remarkable case of liquefying nodular panniculitis in a 33 year old woman, whose lesions were characterized by fluctuation and later by the discharge of large quantities of yellowish brown fluid. The lesions later healed, with depressed scarring of the overlying skin. All bacteriologic studies made on the discharges from these lesions gave negative results. The histologic changes observed in this case appear to us to be identical with those seen in cases of relapsing febrile nonsuppurative panniculitis, and we agree with Binkley⁵ that Shaffer's case may properly be numbered as one of this syndrome in which the lipolytic response was unusually active. Binkley reported the last case in 1939, that of a woman aged 36, with subcutaneous nodules in both breasts and later with similar nodules on the knee and in the groin. The author made the interesting suggestion that some cases of traumatic fatty necrosis of the breast may perhaps fall into this group.

Of the 18 cases reported to date, in 16 the patients have been females and in 2, males. The ages have ranged from 8 years to 56. In 1 of Bailey's cases, that of a woman aged 20, the course was prolonged and rather acutely febrile, with the temperature rising as high as 105 F, accompanied by the usual recurring crops of subcutaneous nodules. The patient died at home over a year after the onset of symptoms, but unfortunately permission for autopsy was refused.

In the first of the 2 cases a complete autopsy was performed eight months after discharge from the hospital.

REPORT OF CASES

CASE 1—L. P., an unemployed Chinese man aged 64, entered the Queen's Hospital on Oct. 22, 1937, complaining of small tender nodules on his trunk and extremities. The lesions were first noticed on the left thigh on Sept. 20, 1937. During the next month they gradually involved the right leg, trunk and arms. The patient's diet for the three weeks prior to his hospitalization had consisted of crackers and water.

Physical examination on admission showed that the patient was emaciated, not acutely ill, but complaining of purple red nodules over the entire body, with the exception of the head and neck (fig. 1). The nodules varied from 1 to 8 cm in diameter. They were firm, tender, discrete and freely movable. The overlying skin to which they were attached was rough and discolored. The mucous membrane was not involved. The pupils reacted sluggishly to light, the teeth were dirty and carious, and the tongue was heavily coated. The heart was enlarged.

4 Shaffer, B. Liquefying Nodular Panniculitis, *Arch. Dermat. & Syph.* **38** 535 (Oct.) 1938.

5 Binkley, J. S. Relapsing Febrile Nodular Nonsuppurative Panniculitis, *J. A. M. A.* **113** 113 (July 8) 1939.

to the left. The heart sounds were of poor quality, but regular, and there were no murmurs. The edge of the liver could be palpated 2 inches (5 cm) below the costal margin.

The temperature was 101 F, the pulse rate was 82 and the respiratory rate 20 per minute. The blood pressure was 185 systolic and 80 diastolic. The peripheral arteries were moderately sclerosed. The red blood cell count was 3,300,000 per cubic millimeter, with the hemoglobin 50 per cent (Newcomer). The white blood cell count was 6,800 per cubic millimeter, and the differential count was within normal limits. The urinalysis showed a specific gravity of 1.015, a heavy cloud of albumin and no sugar. The microscopic examination showed a few coarse granular casts. The blood cholesterol content was 117 mg per hundred cubic centimeters. The Wassermann and Kahn reactions of the blood were negative. The Vidal and Weil-Felix reactions were negative. Two blood cultures were

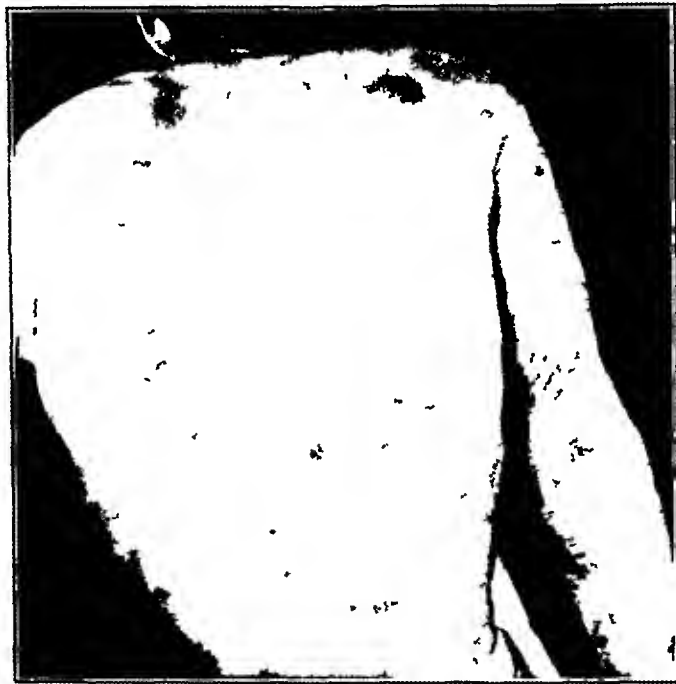


Fig 1 (case 1)—General distribution of the lesions on the back and arms

negative after one week. Repeated examinations of the sputum showed no tubercle bacilli. Smears of skin and scrapings from the nose showed no lepra bacilli. Sternal puncture revealed a normal picture of the bone marrow. Roentgenologic examination of the chest, on two occasions, and of the skull, gastrointestinal tract and long bones showed no abnormalities. Roentgenologic studies of the teeth disclosed an apical abscess of the right lower central incisor and advanced pyorrhea. A biopsy specimen taken October 23 grossly showed the fat of the nodule to be firm, lacking in resilience and waxy. There was a definite line of demarcation between the normal and the diseased tissue (fig 2). The vascularity in the healthy fat was definitely increased around the lesion (fig 3).

The patient's course in the hospital was one of gradual improvement. A temperature of 101 F persisted during the first three weeks of hospitalization, and then the temperature became normal. The nodules gradually became smaller and less painful, and the patient was discharged on November 27, with his cutaneous lesions greatly improved. One transfusion of 550 cc of citrated blood was given.



Fig 2 (case 1) —Photomicrograph showing the involvement of subcutaneous fat. The covering epithelium is approximately normal (Hematoxylin and eosin, $\times 15$)



Fig 3 (case 1) —Photomicrograph showing typical foam cell appearance of degenerating fat cells

His diet was high in vitamins and calories. In addition, he was given three capsules of a combination of liver and stomach extracts and iron (Ilextron) three times a day.

An examination of the patient six weeks after his discharge showed that most of the nodules were completely healed. A few showed central depressed areas. The discoloration in most instances had cleared.

In May 1938 he was brought to the Honolulu Emergency Hospital after having fainted on the street, and since he did not appear acutely ill, he was sent to the Malahua Convalescent Home. Death ensued rather unexpectedly several days later, on May 6, eight and one-half months after the onset of the cutaneous lesions.

Postmortem Observations—The cutaneous lesions had completely disappeared, and except for a few depressed areas no trace of the former widespread involvement could be observed.

The right pleural cavity was obliterated by recent adhesions, and the pleura about the base of the right lung was greatly thickened. The lower lobe of the right lung was noncrepitant and nodular, and the cut surface was studded with solid gray necrotic nodules, with intervening areas of consolidation. The left lung and the upper lobe of the right lung were approximately normal in appearance.

The loops of small bowel were matted together by dense fibrous adhesions, and the peritoneum and mesentery were studded with small white nodules, averaging 1 to 2 mm in diameter. The cut surface of the spleen and liver presented similar nodules, several of those in the liver as large as 1.5 cm in diameter.

The pancreas, adrenals, kidneys, bladder and prostate and the mucous membrane of the stomach and bowel showed no abnormality.

Several blocks of tissue taken from the lower lobe of the right lung revealed an exudative type of tuberculosis with comparatively little fibrosis. Sections from the spleen and liver showed numerous small tubercles, histologically typical in every respect. Sections made through the depressed areas of healed cutaneous lesions showed fibrous replacement of the involved fat.

CASE 2—A P., a Hawaiian woman aged 54, entered the Queen's Hospital on Aug. 14, 1939, complaining of slightly tender nodules on her abdomen and thighs of about three weeks' duration. Her previous diet had been adequate. The family history and her past medical history were irrelevant.

Physical examination revealed that she was well nourished and not acutely ill. The nodules, about twenty-seven of them, ranging in size from 1 by 1 cm to 4 by 4.5 cm, were scattered over the lower part of the abdomen and thighs. They were discrete firm subcutaneous lesions, slightly tender and freely movable, but attached to and involving the overlying skin. The lesions were either slightly raised, roughened and violet blue or depressed, smooth and faintly purple (fig. 4). A few of the nodules were in the path of a superficial vein and grossly involved it. The patient's temperature was 101 F., her pulse rate was 86 and her respiratory rate 18 per minute. There was a congenital deformity of the pinna of the right ear, but otherwise both ears were normal. Examination of the teeth showed marked caries, and both upper cuspids were broken off at the neck. The gums showed extensive pyorrhea. The tonsils were atrophic. The lungs were normal. The heart was enlarged to the left, 3½ inches (9 cm.) from the midsternal line. The sounds were of fair quality, the rhythm, regular. The blood pressure was 140 systolic and 80 diastolic. Abdominal examination gave negative results, and the extremities except for the subcutaneous nodules were normal. Pelvic and rectal examinations showed nothing of clinical importance.

The red blood cell count was 3,700,000 per cubic millimeter, with hemoglobin 56 per cent (Newcomer) The platelet count, bleeding time and clotting time were normal The result of a tourniquet test was negative The urinalysis showed a specific gravity of 1.020 Tests for sugar and albumin gave negative results A blood culture showed no growth in seventy-two hours The sedimentation rate was within normal limits Chemical examination of the blood showed nonprotein nitrogen 40 mg, creatinine 2 mg, sugar (fasting) 89 mg, cholesterol 151 mg and calcium 9.2 mg per hundred cubic centimeters Examinations of the sputum showed no tubercle bacilli Snips of skin and scrapings from the nose were negative for lepra bacilli

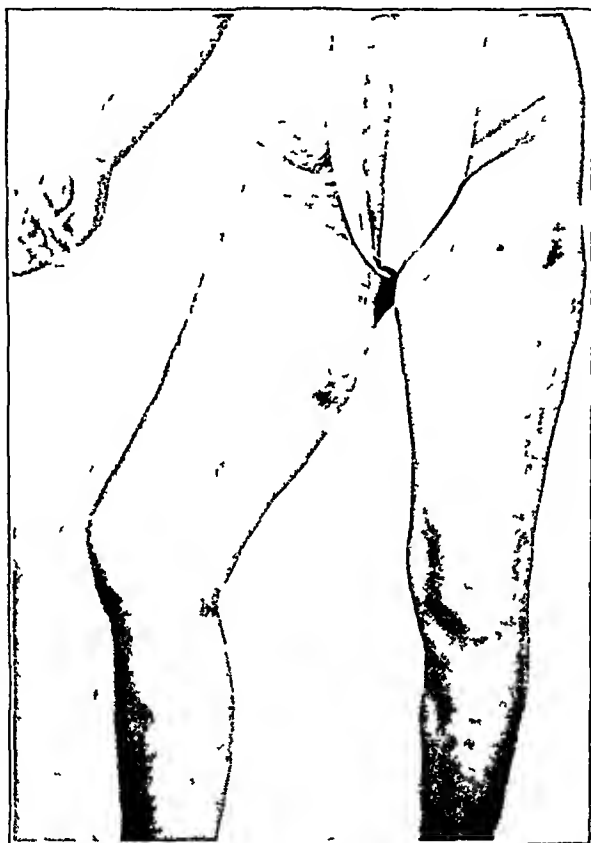


Fig. 4 (case 2) —The lesions on the lower part of the abdomen and the thighs

A roentgenogram of the chest was normal Roentgenologic examination of the teeth showed advanced pyorrhea and abscesses of the apical root of the left bicuspid and the right lateral incisor An electrocardiogram showed a regular sinus rhythm and normal QRS complexes A tuberculin test with purified protein derivative (0.0005 mg in 0.1 cc) gave a negative result A biopsy specimen taken Aug. 16, 1939 showed grossly a similar picture to that described in case 1

The patient's course in the hospital over a period of four weeks was one of improvement, with gradual subsidence of fever and a decrease in the size of the nodules Some healing lesions showed a slight tendency toward central retraction

COMMENT

The autopsy in case 1, performed eight months (May 6, 1938) after the patient's discharge from the hospital, showed disseminated tuberculosis both grossly and microscopically. At the time of his attack of relapsing panniculitis there was no evidence either clinically or roentgenographically of this disease. Erythema nodosum has notably been found associated with tuberculosis, although some authors⁶ have stated the belief that it occurs with other diseases. The pathologic picture of this disease is characterized by dilatation of the capillary plexus, with extravasation of both red and white blood cells. In some

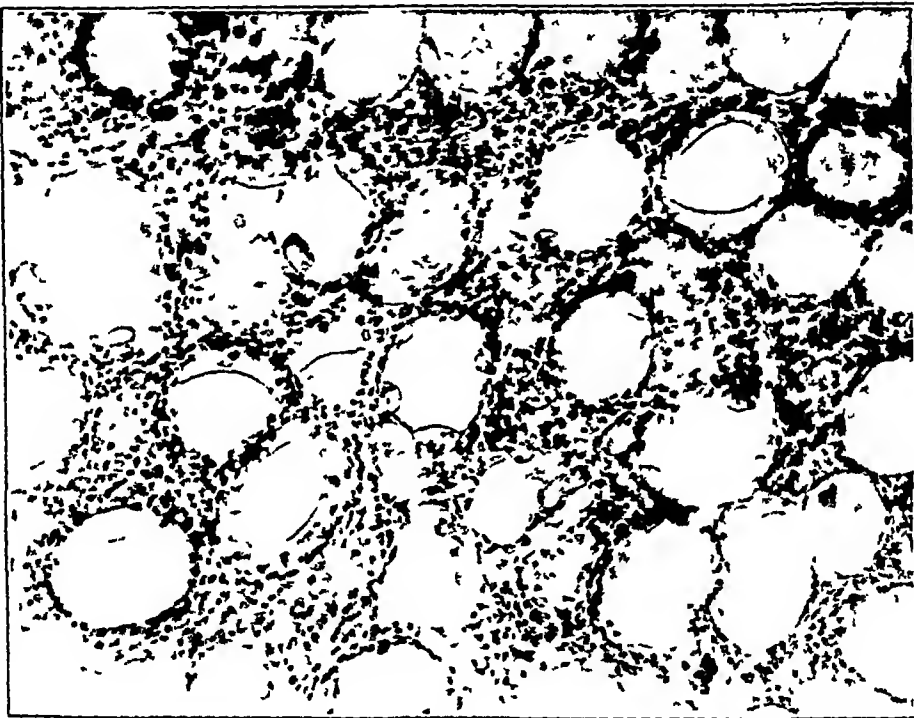


Fig 5 (case 2)—Photomicrograph showing infiltration of inflammatory cells and ingestion of fat by large macrophages, which are often arranged at the periphery of the broken-down fat cell (Sudan III, $\times 400$)

of the capillaries the collection resembles white thrombi. Later in the course of the disease disintegration of the extravasated red cells gives rise to pigmentation. The epidermis is little altered.⁷

This differs considerably from the observations in cases of the Weber-Christian syndrome, in which the pathologic picture is confined to the fatty tissue. Essentially, the microscopic observations showed

⁶ Wallgren A. Rheumatic Erythema Nodosum, *Am J Dis Child* **55** 897 (May) 1938. Erythema Nodosum, editorial *J A M A* **112** 147 (Jan 14) 1939.

⁷ Sutton R. I. *Diseases of the Skin*, St. Louis, C. V. Mosby Company, 1916, p. 114.

the skin to be little altered. In early lesions lipolytic histiocytes appear in the fat spaces and produce a foam cell appearance. Between these fat spaces lymphocytic infiltration is seen. As time goes on the foam cells regress, and the nuclei tend to fuse, giving the appearance of giant cells (fig 5). As this is taking place the stroma becomes more densely infiltrated with lymphocytes and mononuclear cells, which obliterate the empty fat spaces. An interesting early finding is the swelling and thrombosis of the smaller blood vessels. The larger arterioles show edema of the muscularis with decided endothelial proliferation. Around the larger venules definite lymphocytic infiltration is seen. These changes are noted early and persist in the older lesion.

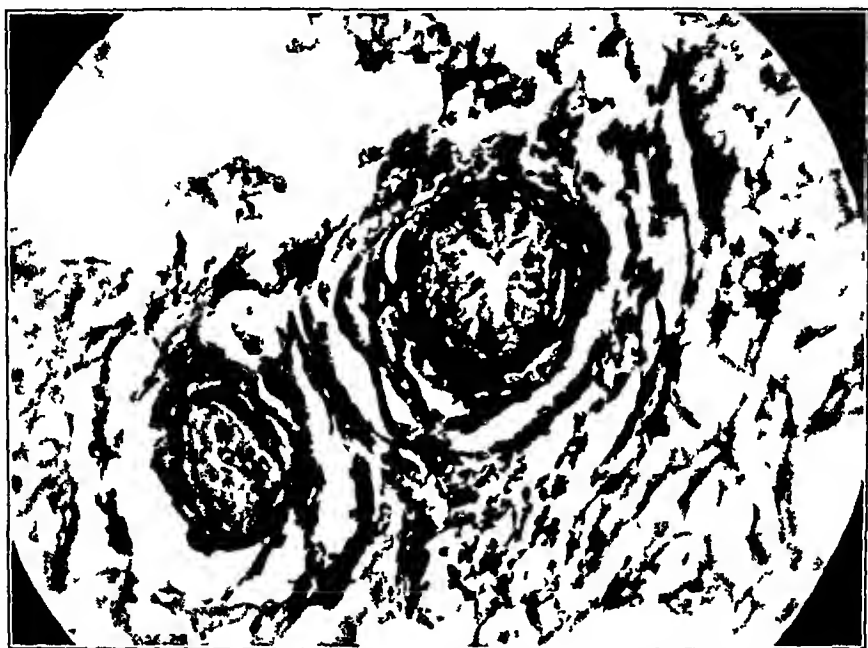


Fig 6 (case 1) —Photomicrograph showing edema of the walls of the larger arterioles, with endothelial proliferation (Weigert's stain, $\times 400$)

They form an essential part of the pathologic picture (fig 6). The last stage is fibrosis with healing.

This type of reaction is not specific for this disease, since it has been described as following injections of carcinogenic agents in experimental research on cancer⁸. It may also be classified essentially as a foreign body type of reaction.

8 Orr, J. W. An Investigation of the Histological Changes in the Subcutaneous Tissues of Mice During the Induction of Sarcoma by Carcinogenic Hydrocarbons, *J. Path. & Bact.* 49:157 (July) 1939.

Apparently the amount of depression of a lesion following healing is dependent on the amount of fatty destruction. In both cases reported central depression occurred only in the larger lesions.

No cause of the disease could be discovered. Both patients had abscessed teeth. One had lived on a vitamin-deficient diet over a long period, while the other had had an adequate intake of vitamins.

SUMMARY

Two cases of relapsing febrile nodular nonsuppurative panniculitis are added to the 18 already reported. One patient was a man aged 64, and the other, a woman aged 54.

No definite etiologic factors were discovered.

NITRITOID REACTION TO TRYPARSAMIDE

REPORT OF A CASE

HERMAN A LEVY, MD

CHICAGO

Vasomotor reactions not uncommonly occur to the arsenicals used in the treatment of syphilis, especially to the trivalent arsphenamines. The pentavalent tryparsamide, however, rarely produces ill effects. Moore¹ stated that "visual damage is the only complication of tryparsamide therapy to be feared." With 6,933 injections of tryparsamide given by the medical department of the United States Navy,² only 1 untoward result occurred—a mild exfoliative dermatitis. A thorough search of the literature revealed a paucity of reports of vasomotor reactions to this drug. A suggestive report was that of Miller and O'Donnell,³ whose patient suffered a profound collapse with generalized pallor of the skin, rather than the rubor associated with the so-called nitritoid reaction. Recently, however, Astrachan and Franks⁴ reported a typical nitritoid reaction in a 32 year old woman and also referred to two previous reports.⁵ According to Stokes⁶ and O'Leary,⁷ this reaction is very uncommon. Other untoward effects from this useful drug, including injury to the optic nerve,⁸ dermatitis,⁹ psychosis¹⁰ and herpes

From the Department of Medicine, University of Illinois College of Medicine

1 Moore, J. E. *The Modern Treatment of Syphilis*, Springfield, Ill., Charles C. Thomas, Publisher, 1933.

2 Phelps, J. R., and Washburn, W. A. *Toxic Effects of Arsenical Compounds Employed in the Treatment of Syphilis in the United States Navy*, *Urol & Cutan Rev* **34**:458 (July) 1930.

3 Miller, J. K., and O'Donnell, H. J. *Sensitivity to Tryparsamide*, *Arch Dermat & Syph* **35**:264 (Feb) 1937.

4 Astrachan, G. D., and Franks, A. G. *Nitritoid Reaction Following an Injection of Tryparsamide*, *Arch Dermat & Syph* **38**:949 (Dec) 1938.

5 O'Leary, P., and Becker, S. *Further Observations on the Treatment of Neurosyphilis with Tryparsamide*, *M J & Rec* **123**:305 (March 3) 1926. Silvers-ton, J. D. *Observations on Tryparsamide Therapy in Neurosyphilis*, *Lancet* **2**:695 (Oct 2) 1926.

6 Stokes, J. H. *Personal communication to the author, February 1938.*

7 O'Leary, P. A. *Personal communication to the author, February 1938.*

8 Mayer, L. L. *Tryparsamide Therapy of Neurosyphilis and Atrophy of the Optic Nerve*, *J A M A* **109**:1793 (Nov 27) 1937.

9 Bragman, L. J. *Tryparsamide Dermatitis. Report of a Case and Survey of Literature*, *Am J Syph & Neurol* **18**:308 (July) 1934.

10 Hoverson, E. T. *Psychosis Associated with the Administration of Tryparsamide*, *Am J Syph & Neurol* **19**:217 (April) 1935.

zoster,¹¹ are not common but do occur. The occurrence of a typical, severe nitritoid crisis following tryparsamide treatment in a patient with an early stage of dementia paralytica is worthy of note.

REPORT OF CASE

A 53 year old white man had been receiving treatment for early dementia paralytica since April 1937. The clinical picture consisted of a mild depressive state, intermittent headaches and nerve deafness, associated with Argyll Robertson pupils, absence of atrophy of the optic nerves, slowness of speech, greatly increased deep reflexes and absence of abdominal reflexes. The Wassermann and Kahn reactions of the blood were positive. Spinal puncture yielded a clear fluid, under moderately increased pressure, with 29 cells per cubic millimeter and a slightly positive reaction to the Pandy test. The Wassermann and Kahn reactions were positive with 0.2 cc of fluid, the colloidal gold curve formula was 3333322111. There was no evidence, subjective or objective, of associated cardiovascular syphilis.

Previous treatment, all well tolerated, consisted of the oral administration of iodides, intramuscular injections of bismuth preparations both water and oil soluble, ten injections of mapharsen and ten artificial fever treatments by means of a cabinet and short wave diathermy. Weekly intravenous injections of 2 Gm of tryparsamide were made, the first six of which were given just before the last six fever treatments were started.

One minute after the thirteenth injection had been completed, marked erythema of the face and ears appeared, followed by similar changes in the neck, arms, hands, trunk and lower extremities. In the wake of the rubor followed marked perspiration. During the cutaneous reaction, which lasted about two minutes, the patient was nauseated and alarmingly weak. Vomiting occurred about three minutes after the changes in the skin had disappeared. The pulse remained strong and rapid, but the blood pressure dropped to 80 systolic and 50 diastolic (normally 120 to 130 and 70 to 80). The picture was that of profound generalized vasodilatation, especially of the skin. Treatment consisted of the subcutaneous injection of 0.6 cc of a 1:1,000 solution of epinephrine hydrochloride, and this was repeated later. Recovery seemed complete within an hour. However, one hour later a milder attack, of shorter duration, occurred. There were no further symptoms or any late bad effects. On the advice of Stokes⁶ and O'Leary,⁷ I expected to resume treatment with a smaller dose after a month's vacation, but the patient refused further medication "in the vein." He is now receiving iodides and heavy metals.

SUMMARY

The rare occurrence of a severe nitritoid reaction after tryparsamide therapy is reported.

¹¹ Rosenberg, W. A. Bilateral Asymmetrical Herpes Zoster (Following Tryparsamide Therapy), *Illinois M. J.* 74:164 (Aug.) 1938.

CUTANEOUS ABSORPTION

I A DIRECT TECHNIC FOR DEMONSTRATING THE PERCUTANEOUS ABSORPTION OF ANTIGENS

ABRAHAM WALZER, M D

BROOKLYN

Up to the present time, most of the substances administered by injection to human beings and animals for therapeutic or experimental purposes have been drugs. These have varied from such simple elements as mercury, lead and arsenic to more complex substances, such as alkaloids, histamine and the essential oils. Recently endocrine substances, vitamins, toxins, antitoxins and bacterial vaccines have also been administered percutaneously by injection, with variable results.

The procedures employed by different observers to determine percutaneous absorption have at times been complicated. Some investigators have relied on prolonged clinical observations of the pharmacologic, toxic or therapeutic effects of the applied agent to establish its absorption. Others have performed extensive chemical examinations of blood, urine or tissues to detect the presence of the absorbed substance. Immunologic methods have also been employed to show the absorption of antigens through the skin. These have included the formation of specific antibodies, the anaphylactic sensitization and shocking of animals and the immunization of human beings and animals against various diseases, as diphtheria, scarlet fever, typhoid fever, tetanus, paratyphoid fever and dysentery.

The present communication describes a simple technic which demonstrates that proteins rubbed into the skin readily pass into the circulation. The technic is based on an immunologic principle. It is a direct method of detecting almost immediately the entrance into the circulation of the externally applied antigen. In the studies cottonseed and peanut were the protein antigens employed.

TECHNIC

The technic is similar to the one employed by Walzer¹ in his studies on the absorption of undigested proteins into the circulation through various channels.

Read at the fourth semiannual meeting of the Allergy Division of the Jewish Hospital on May 16, 1938.

From the Department of Dermatology and Syphilology and the Department of Allergy of the Jewish Hospital.

1 Walzer, M. Studies in Absorption of Undigested Proteins in Human Beings. I. A Simple Direct Method of Studying the Absorption of Undigested Proteins, *J Immunol* **16** 143, 1927.

Briefly stated, the technic consists first of passively sensitizing a site on the skin to an antigen. After twenty-four or forty-eight hours, the antigen is rubbed in at another cutaneous site. The lighting up of the sensitized site with an urticarial reaction marks the entrance of the antigen into the circulation.

The serum for sensitization was obtained from sensitive patients who showed marked reactions to cutaneous tests with cottonseed. A serum from a peanut-sensitive patient was also used in some of the experiments. Most of the studies, however, were carried out with a serum in which the titer of the reagins for cottonseed was high. The serum was used undiluted in the monkeys and in a dilution of 1 to 4 in the human subjects. From 0.05 to 0.1 cc. was injected intracutaneously for local passive sensitization.

The antigen was prepared in the following manner. One or 2 Gm. of dehulled cottonseeds were vigorously triturated in a mortar with a pestle until they were reduced (in about five minutes) to a gummy mass. This was then incorporated in an equal amount of a grease, such as petrolatum. The portion for injection in a monkey weighed 2 Gm., and in a human subject, 4 Gm. In some of the experiments on monkeys it was found that larger doses of the antigen were absorbed more quickly. Hence in one series of animals portions weighing 4 Gm. were used.

DEMONSTRATION OF ABSORPTION OF PROTEIN THROUGH THE SKIN

The human subjects were adults free of dermatologic disturbances and with no history of atopic illnesses, such as asthma and hay fever.

On the day previous to the injection sensitization was accomplished by the injection of 0.05 cc. of the diluted serum either on the upper part of the arm or on the forearm. The injection of the antigen in the vehicle was performed on the corresponding part of the opposite extremity. This area was not previously washed or otherwise prepared. Small portions of the ointment were applied at short intervals, and the rubbing was done in a slow but forceful manner. Fifteen minutes was the time arbitrarily decided on for the injection, but the procedure was discontinued at the first indication of a reaction at the sensitized site.

The reaction at the sensitized site in the human subjects began with an itch and faint erythema usually from twelve to twenty minutes after the onset of the rubbing (table 1). Then a wheal rapidly developed within the erythematous area. A completed reaction was a wheal typical of urticaria vulgaris and similar in development, course and regression.

to the experimental wheal previously described by M Walzer and A Walzer² in their studies on urticaria

Evidences of irritation occurred at some of the massaged areas, especially on those having pronounced lanugo hair. Erythema and many follicular punctate purpuric points developed after the rubbing. There was also some pruritus. The irritation was attributed to the pronounced lanugo hair, the forceful rubbing or the irritative action of theunction

In the *Macacus rhesus* monkeys corresponding parts of both thighs, usually the lateral surfaces, were carefully shaved forty-eight hours before the experiments were begun. One of the sites was then sensitized by the intracutaneous injection of 0.05 cc of undiluted serum. The area was marked off with ink. Two days later the antigen in the grease vehicle was firmly but slowly rubbed on the other shaved thigh. Rubbing was continued for fifteen minutes or until the onset of a reaction at the sensitized site on the opposite thigh.

TABLE 1—*The Percutaneous Absorption of Cottonseed Antigen in Human Subjects*

| Name | Date of Sensitization | Site of Sensitization | Date Antigen Applied | Site Rubbed | Rubbing Time, Minutes | Reaction Time, Minutes |
|------|-----------------------|-----------------------|----------------------|-------------|-----------------------|------------------------|
| J O | 2/ 5/38 | Right arm | 2/ 6/38 | Left arm | 15 | 20 |
| M L | 2/ 5/38 | Left arm | 2/ 6/38 | Right arm | 13 | 13 |
| E H | 2/12/38 | Right arm | 2/13/38 | Left arm | 12 | 12 |
| H N | 2/12/38 | Left arm | 2/13/38 | Right arm | 15 | 19 |
| W A | 2/12/38 | Left arm | 2/13/38 | Right arm | 15 | 16 |

The occurrence of the reaction at the sensitized site in monkeys has previously been described by Straus³. Some variations from the typical reaction in the present studies were noted. However, the common reactions were the formation of goose skin, blanching and induration. The most common type of reaction began with the development of a group of pinpoint-sized slightly elevated points at the hair follicles having the appearance of cutis anserina. They usually appeared at or around the sensitized site from six to sixteen minutes after the onset of the rubbing (table 2). Within a minute or two the affected area became ivory white and slightly elevated. The reaction rapidly progressed by the peripheral increase in the number of tiny raised follicular

2 (a) Walzer, A., and Walzer, M. Studies in Urticaria. I. Wheal Production Through Internal Channels, *Am J M Sc* **173** 270, 1927, (b) Urticaria II. Experimental Wheal Produced on Normal Skin Through Internal Channels, *Arch Dermat & Syph* **17** 659 (May) 1928. (c) Walzer, A. Urticaria. IV. Wheal Formation on Abnormal Skins, *ibid* **20** 277 (Sept.) 1929.

3 Straus, H. W. Studies in Experimental Hypersensitiveness in the Rhesus Monkey. II. Passive Local Cutaneous Sensitization with Human Reaginic Sera, *J Immunol* **32** 251, 1937.

points and by the extension of the blanching. In from five to twenty minutes the reaction was at its height. A completed reaction in the experiments was a lesion varying from 1 by 1.5 cm to 3 by 5 cm which was sharply outlined, faintly raised, decidedly indurated and ivory white, with a smooth surface and a sharp, almost straight border. No preliminary central or secondary surrounding erythema was observed. Pruritus seemed to be slight or absent, but it was difficult to evaluate this feature because the animals were tied down during the development of the reaction and could therefore make no attempt at scratching.

A number of variations were noted in the development of the reactions. In some instances the goose skin and the blanching were absent, the reaction being a sharply outlined smooth, raised, indurated lesion. Occasionally many of the goose skin papules persisted, giving a rough-

TABLE 2—*The Percutaneous Absorption of Cottonseed Antigens in Monkeys*

| Number | Date of Sensitization | Site of Sensitization | Date Antigen Applied | Site Rubbed | Amount of Antigen, Gm | Rubbing Time, Minutes | Reaction Time, Minutes |
|--------|-----------------------|-----------------------|----------------------|-------------|-----------------------|-----------------------|------------------------|
| 7 | 3/22/38 | Left thigh | 3/24/38 | Right thigh | 1 | 14 | 14 |
| 10 | 3/22/38 | Left thigh | 3/24/38 | Right thigh | 1 | 8 | 8 |
| 10 | 3/29/38 | Right thigh | 3/31/38 | Left thigh | 1 | 11 | 11 |
| 18 | 3/29/38 | Right thigh | 3/31/38 | Left thigh | 1 | 9 | 9 |
| 2 | 4/18/38 | Right thigh | 4/20/38 | Left thigh | 1 | 15 | 16 |
| 34 | 6/28/39 | Right thigh | 6/30/39 | Left thigh | 2 | 15 | 6 |
| 17 | 6/28/39 | Left thigh | 6/30/39 | Right thigh | 2 | 10 | 10 |
| 19 | 7/11/39 | Right thigh | 7/12/39 | Left thigh | 2 | 11 | 11 |
| 53 | 7/11/39 | Right thigh | 7/12/39 | Left thigh | 2 | 8 | 8 |
| 38 | 7/17/39 | Right thigh | 7/19/39 | Left thigh | 2 | 6 | 6 |
| 36 | 7/17/39 | Left thigh | 7/19/39 | Right thigh | 2 | 7 | 7 |

ened rather than a smooth surface to the lesion. A serrated border was present in some of the reactions. The amount of elevation also varied, and occasionally this feature was absent. In some instances a diffuse blanching was the first indication of the developing reaction. At other times blanching at the hair follicles first appeared as white points, which then increased in size and merged to form a single white patch, with or without goose skin lesions surrounding it.

The reaction as it appeared in the monkeys therefore differed in some respects from the typical wheal as seen in human beings. Straus⁴ suggested that the sudden erection of the hair follicles with the resulting goose skin was the equivalent of the primary erythematous phase of the reaction preceding the appearance of the wheal in human beings. The indurated, raised and blanched lesion in the monkey, however, is suggestive of the wheal in man. Grayzel and Walzer⁴ have shown that

⁴ Grayzel, D., and Walzer, M. The Pathology of the Allergic Reaction in the Passively Sensitized Tissues of the Macacus Rhesus Monkey, *J Allergy* 10: 478, 1939.

histologically the reaction in monkeys closely simulates the one in human beings

The following protocol is a chronologic description of a typical experiment on a monkey, including details of the progressive development of the most common type of reaction

MONKEY 18—On April 12, 1938, both thighs were shaved, and a site on the right thigh was sensitized by the intracutaneous injection of 0.05 cc of human serum obtained from a cottonseed-sensitive patient

The following observations were made on April 14

11 40 a m Two grams of the minction, consisting of equal parts of cottonseed and petrolatum, were slowly rubbed in small increments on the shaved part of the left thigh

11 49 a m Tiny skin-colored pinpoint papular elevations appeared at the hair follicles of the sensitized area

11 51 a m Blanching of the sensitized area was noted over a patch which measured 1.25 by 1.5 cm. The blanched area presented a sharp, even border and a goose skin surface and was definitely indurated

11 55 a m The goose skin had disappeared. The blanched area was ivory white, slightly elevated and indurated. The surface was smooth, and the border was sharp and raised. The reaction was at its height

12 00 The center of the reaction seemed to be a little more raised than the borders, otherwise the lesion was unchanged

12 10 p m The blanching had diminished somewhat

12 20 p m The blanching and induration were considerably less pronounced

12 30 p m The blanching and induration continued to diminish, but the reaction was still fairly distinct

The following protocol is a chronologic description of an experiment on another animal, illustrating one of the atypical forms of reactions encountered

MONKEY 38—On July 17, 1939, both thighs were shaved, and a site on the right thigh was sensitized by the intracutaneous injection of 0.05 cc of serum obtained from a cottonseed-sensitive patient

The following observations were made on July 19

1 42 p m Four grams of minction, consisting of equal parts of cottonseed and petrolatum, were slowly rubbed in small increments on the shaved surface of the left thigh

1 48 p m Tiny white follicular raised points appeared at the sensitized site on the opposite thigh, giving it the appearance of goose skin

1 50 p m The blanching around the raised follicular points had increased in intensity and in size

1 51 p m All the white spots had joined, forming one white patch, 1.5 by 1.5 cm

1 53 p m The blanching had extended beyond the boundaries of the original sensitized site. Goose skin lesions had not preceded the blanching in the outer areas. The patch was somewhat indurated. Raised follicular points were still present in the center

1 56 p m The lesion had grown considerably in size, especially in length. Only an occasional raised follicular point was noted in the peripheral area. The papules in the center had partially disappeared.

1 58 p m The lesion had enlarged to about 5 by 3 cm. It was definitely indurated, elevated, sharply demarcated and ivory white. The goose skin was present only in the center.

2 05 p m With the exception of the increase in blanching, the reaction was the same as described for 1 58 p m. It had reached the height of its development.

2 09 p m The lesion seemed to be higher in the center than at the periphery, presenting a dome-shaped appearance. This was an indication that regression had begun. The goose skin, however, was still present but not so pronounced as previously.

2 10 p m The blanching had diminished, and the goose skin lesions had flattened considerably. The induration and elevation were still pronounced.

2 13 p m The goose skin had disappeared, the induration had decreased.

2 23 p m A pale slightly indurated patch was all that remained of the lesion.

2 49 p m The induration had gone. Only a slight blanching was still present.

3 00 p m The site was practically normal again.

COMMENT

A protein, finely triturated and suspended in a grease base, was absorbed into the circulation in human beings and in monkeys after it was rubbed into the skin. Absorption was marked by the reaction which developed at a passively sensitized site in a distant area.

Proteins have previously been administered through the skin, and the evidence of their absorption has in some instances been based on immunologic principles. The percutaneous absorption of toxins, for example, was demonstrated by the eventual disappearance of positive Schick and Dick reactions in patients so treated. The cutaneous absorption of tetanus antitoxin was demonstrated by the neutralization of the tetanus toxin as a result of the rubbing in. Likewise the absorption of vaccines of typhoid and paratyphoid bacilli was indicated by the subsequent appearance of corresponding antibodies in the circulation of persons who were treated in this manner. With other proteins, such as insulin, the cutaneous absorption was proved by chemical, physiologic or therapeutic analysis or by the demonstration of its effects in treated subjects.

All these methods of determining the absorption of protein through the skin require complicated technical procedures and yield information only indirectly and after a considerable delay. The technic here presented, on the other hand, is direct. It gives the desired information almost immediately. Moreover, it is simple and harmless. It is equally

applicable to human beings and to *Macacus rhesus* monkeys. Being immunologic in principle, however, the technic is limited in its application. It may be employed only for antigens for which strong reaginic serums are obtainable.

Further studies in cutaneous absorption dealing with the various factors concerned in this mechanism will be presented in future publications.

SUMMARY

A simple, direct and harmless technic, based on immunologic principles, for demonstrating the absorption of protein antigens through the skin is presented.

The technic is applicable to human beings and to *Macacus rhesus* monkeys.

PRURITUS ANI AND ITS RELATIONSHIP TO SEBORRHEIC ECZEMA AND DERMATOPHYTOSIS

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AND
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LOS ANGELES

It has been noted independently by both of us that a definite relationship exists between many attacks of pruritus ani and exacerbations either of seborrheic eczema of the scalp, ear canals, eyelids, umbilicus or axillas or of dermatophytosis of the feet. What relationship exists between these conditions and how to determine the exact status of one to the other are problems which become increasingly difficult, because of the multiplicity of theoretic, physical and personal problems involved. We have attempted, by the use of material gathered from other published work and from our own observations of 145 cases of pruritus ani, to explain on an allergic basis what seem to be the fundamental factors involved in anal itching.

In view of the difficulty experienced in gaining the cooperation of the patient when the primary focus alone was treated without giving some immediate relief to the pruritus, we thought it advisable to treat both the distant and the local involvement until a symptomatic cure was obtained. The patients were then carefully instructed to watch for recurrent symptoms of pruritus ani, seborrheic eczema or dermatophytosis and to report immediately for observation. The result of these observations will be presented in detail later in the paper.

REVIEW OF THE PERTINENT LITERATURE

The literature has been combed rather thoroughly, but we have been unable to find any instance in which pruritus ani was the result of an allergic reaction to seborrheic eczema or dermatophytosis. Caskey¹ listed 34 causes of pruritus ani but did not mention any relation to the aforementioned allergic factor.

Early in the century Castellani pointed out the connection between pruritus ani and fungous infections. A more recent review of the

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¹ Caskey C R. Pruritus Ani, California & West Med 50 14 (Jan) 1939

subject by Castellani² covered the subject in more detail. He stated "Pruritus ani of mycotic origin is a condition, as a rule, which resembles a form of latent epidermophytosis of the ano-perianal region without the usual 'objective symptoms' of an ordinary active epidermophytosis being present." He was able to culture some form of yeast in only about 30 per cent of his cases. Terrell and Shaw³ expressed the opinion that pruritus is not of fungous nature in all cases, but they were forced to the conclusion that in the majority of the cases it is primarily due to a fungus. They reported 54 cases with 36 cures obtained with anti-fungicidal therapy. Kiger was quoted by Goldman⁴ as suggesting that a definite distal focus of infection causes pruritus in many cases. Scarborough⁵ stated emphatically "Experience has shown that there is always a local cause for the symptom of localized anal itching." He reviewed Chope's work on 11 selected cases in which it was felt that the pruritus was definitely of fungous origin and in which the clinical appearance was characteristic. Scarborough and Chope were able to demonstrate the existence of myceliums in 3 cases. In no case could they culture a fungus on Sabouraud's culture medium. They stated that they were unable to stop the itching in a single patient by local treatment but that they were successful when the underlying pathologic conditions had been removed. Tucker and Hellwig⁶ observed nothing which would suggest that pruritus ani has a bacterial or a parasitic cause. They expressed the opinion that skatole and possibly other hydrocarbons present in human feces can, under certain circumstances, act as the etiologic agent. It seems that most authors attribute all itching to the one cause that happens to be "their particular hobby."

PRURITUS ANI CONSIDERED AS A POSSIBLE ALLERGIC PHENOMENON

We feel that there are many causes of pruritus ani, both local and constitutional, however, we feel that frequently pruritus ani is a toxic or an allergic manifestation of seborrheic eczema or of dermatophytosis, in the same manner in which the well recognized dermatophytid of the hands is a manifestation of dermatophytosis. In many cases the pruritus

2 Castellani, A. Pruritus Ani and Pruritus Vulvae of Mycotic Origin, *Practitioner* **117** 341 (Dec) 1926

3 Terrell, E. H., and Shaw, F. W. Observations of Fungal Infections of the Peri-Anal Skin and Rectum, *South M. J.* **21** 61 (Nov) 1928

4 Goldman, C. Pruritus Ani—Its Etiology and Treatment, *M. J. & Rec* **122** 88 (July) 1925

5 Scarborough, R. Pruritus Ani Its Etiology and Treatment, *Ann Surg* **98**.1039 (Dec) 1933

6 Tucker, C., and Hellwig, C. Pruritus Ani Histologic Picture in Forty-Three Cases, *Arch Surg* **34** 929 (May) 1937

begins with localized itching, tingling, tickling, biting, picking, pricking, creeping, crawling or burning sensations as the only symptoms, later to develop into dermatitis or eczema, as the physical changes become more apparent. The pruritus is in itself not a disease but a symptom complex brought on by irritation of the nerve endings. Clinically the pruritus is manifested by erythema, by the appearance of papules and vesicles, by maceration of the tissue, by fissures and, in extreme cases, by eczematization, oozing, crusting and scaling. The itching is frequently extremely severe, occurring in paroxysms which are uncontrollable and which cause the patient untold embarrassment, occasionally leading to nervous breakdowns and seriously affecting the general health. It has been our experience that this condition of allergy, sensitivity or irritability varies with each patient. Some patients with severe external dermatitis suffer less than others with no visible clinical manifestation of the condition. However, it would appear that in most patients an ever increasing hypersensitivity develops, and eventually a psychoneurosis.

Fungous and bacterial infections, especially when associated with intertrigo, itch severely. The infections apparently set up an epidermal hypersensitivity which manifests itself in areas where there is moisture, irritation or pressure. Bloch⁷ and Sulzberger⁸ explained the physiologic mechanics of the "ids" as they are understood today. They stated that fungi or bacteria originating from a focus or from foci of infection can enter the blood stream and be distributed to the skin, where they are rapidly killed, an altered condition of the skin or "allergy" being caused, so that on future contact of the skin with the organisms or their products varying types of reaction are produced, from simple pruritus to eczema. This is the reaction observed in dermatophytids and bacteriids, as contrasted with the condition at the primary focus of infection. It is therefore possible that in one of two conditions which appear to be similar, the primary focus, the organism may be found, while in the other, the secondary manifestation, the organism is rarely found. Immunologically, this allergic reaction can be verified by inoculation with vaccines of the offending organism, which will demonstrate the altered reaction of the skin, showing that the skin reacts to the toxins of the primary infection as well as to the organism itself.

The foregoing data have been given to correlate briefly our understanding of "allergy" in its relation to the "ids" and to show how it would be possible to include pruritus and as a toxic manifestation of seborrheic eczema and dermatophytosis.

7 Bloch, B, in Jadassohn, J. Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol 11, p 564.

8 Sulzberger, M. B. The Pathogenesis of Trichophytids, Arch Dermat & Syph 18 891 (Dec) 1928.

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ETIOLOGY OF SEBORRHEIC ECZEMA

The etiology of seborrheic eczema has been in dispute since Malassez⁹ first described the organism he called *Pityrosporum ovale* in 1874. Many authorities have failed to obtain a pure culture, however, Moore, Kile and Engman¹⁰ were successful not only in cultivating a pure strain but in reproducing a patch of seborrheic eczema in a test subject. It should be noted that in reproducing the disease only patients with seborrhea elsewhere than on the scalp were used, which indicates that there may be other basic factors involved in the disease. It is accepted that the average patient with seborrheic eczema has a peculiar pathologic skin of an edematous type, associated with an exudative diathesis of the tissues. The skin of these patients with seborrheic eczema frequently presents a fatty or waxy appearance. It is intolerant of excessive amounts of carbohydrates and fats. This condition would indicate that persons with seborrheic eczema could have toxic eruptions originating on the principles of the dermatophytids and bacterids which possibly should be called "pityrosporids" or seborrheids. It should be noted that Moore, Kile and Engman were able to produce a vaccine which they called pityrosporin.

Those interested in the organisms which live in symbiosis with *Pityrosporum ovale* and which produce different clinical manifestations of seborrheic eczema, such as *Staphylococcus albus*, *Staphylococcus epidermidis* and *Staphylococcus aureus*, are referred to an excellent article by MacKee and Lewis¹¹.

FACTORS INVOLVED IN THE DEVELOPMENT OF PRURITUS ANI

When pruritus ani arises as a secondary toxic or allergic reaction to the primary dermatophytosis or to seborrheic eczema, by the nature of the anatomy of the anus it is in a position to become invaded by a variety of organisms. The yeast organism *Monilia* is frequently found in culture, as well as the various types of pyogenic bacteria constantly present on the body. Therefore, even though the original pruritus is allergic in nature, there may and usually does occur secondary infection. This element of actual infection, as well as the primary focus, must be eliminated when one is treating the condition. There are other factors to be considered, such as scratching, mechanical abrasion of the part by rough clothing or toilet paper, perspiration and anything else which

9 Malassez, L. Note sur le champignon de la pelade, Arch de physiol norm et path 6 203, 1874

10 Moore, M., Kile, R. L., Engman, M. F., Jr, and Engman, M. F. Etiology and Pathology of Seborrheic Dermatitis, Arch Dermat & Syph 33 457 (March) 1936

11 MacKee, G., and Lewis, G. Dandruff and Seborrhea. Flora of "Normal" and Diseased Scalps, J Invest Dermat 1 131 (April) 1938

destroys or damages the lower layers of the epidermis or papillary bodies. These factors must of necessity be taken into account when therapy is considered.

The skin loses its resistance after repeated injuries, whether they result from the original id, from the secondary infection or from mechanical or physiologic factors. It is necessary to eliminate all of the causes of the pruritus before a good result can be expected. Removing one or more of the predisposing factors would still allow the pruritus to continue.

REPORT OF CASES

We shall report our observations on 145 patients with pruritus ani and attempt to show its possible relationship to two common cutaneous diseases, seborrheic eczema and dermatophytosis. Because of incomplete records in some instances, failure of some patients to continue treatment and failure of the authors to coordinate their records until late in the series, there have arisen some discrepancies.

Dermatologic Series—This series of cases was viewed from the dermatologic standpoint (P D F), and therefore attention was directed to other clinical cutaneous manifestations than the pruritus. This series tended to include a higher percentage of patients with seborrheic eczema and dermatophytosis than the corresponding proctologic series. Only patients under observation for a considerable period were included in this series. All patients seen only in consultation were excluded.

Forty-four patients with pruritus ani are presented for consideration. Nineteen had definite clinical manifestations of seborrheic eczema of the scalp, ears, eyebrows, eyelids, chest, axillae or umbilicus. Thirty-one presented the usual objective symptoms of dermatophytosis, confirmed by extemporaneous microscopic examination in 22 cases.

In the 9 cases in which immediate microscopic examination gave negative results, material was cultured on Sabouraud's medium. In 4 of these cases the cultures yielded fungi. It was observed on the first examination that 15 patients had both seborrheic eczema and dermatophytosis.

All the patients except 2 were placed on a regimen of intensive treatment for both the local and the possible primary foci of infection. The 2 patients who were not treated locally for the pruritus were persons belonging to the medical profession who had noted for themselves the relationship of the pruritus, in 1 instance to dermatophytosis and in the other to seborrheic eczema. Both of these persons had complete amelioration of their symptoms of pruritus ani when treated solely for the primary cause.

Fourteen of the remaining 42 patients in the series had symptoms which were considered to be caused purely by local factors, and 6 patients were referred to one of us (M R H) for removal of definitely pathologic tissue. Twenty-eight patients were cured of their symptoms of pruritus by the treatment advocated in this paper.

Pruritus ani recurred after the apparent symptomatic cures in 22 of the 28 patients. The recurrence was definitely associated with seborrheic eczema in 7 of the patients, or 32 per cent, with dermatophytosis in 15, or 68 per cent, and with a combination of the two conditions in 5, or 23 per cent.

The patients in this series were given a soothing powder for the pruritus and active treatment was instituted for the complicating seborrheic eczema or dermatophytosis. Of the 10 patients with recurrences who were treated only for der-

matophytosis, 8 patients showed apparent symptomatic cures, some of these patients had numerous recurrences for which only the feet were treated, and the pruritus subsided. The 7 patients in whom a relapse was noted in conjunction with an exacerbation of seborrheic eczema were treated only for the seborrheic eczema, and 5 apparent symptomatic cures were effected. In the remaining 5 patients in whom the relapse was associated with both seborrheic eczema and dermatophytosis, 3 symptomatic cures were effected by treatment of the associated conditions only. Therefore, in 22 patients in whom recurrences of pruritus ani were associated with either seborrheic eczema or dermatophytosis or both, 16 symptomatic cures were effected by treating only the primary source of the allergy or "id." Proper hygiene of the anus and a soothing talcum powder were used in all cases.

Proctologic Series—In a series of 101 patients observed by one of us (M. R. H.), pruritus ani was one of the main complaints for which proctologic consultation was sought, 34 patients were examined and a consultation report was rendered. A group of 20 patients in this series showed evidence of active mycotic lesions on their feet. Seborrheic eczema was not considered as a possible causative factor by this author until about three years ago. Therefore, only 1 of the 20 patients already mentioned was noted as having seborrheic eczema of the scalp and ears.

In another group of 8 patients in this series, there was no evidence of mycotic activity, but 2 patients did give a previous history of fungous infection. Surgical treatment of the existing anorectal disease was recommended. These patients did not return for further care.

In a third group in this series, 37 patients in all, medical treatment alone was administered. Thirty-two patients gave evidence of active mycotic infection of their feet. Six of these 32 patients had coexisting seborrheic eczema. One of the 5 patients who gave no evidence of active mycosis had a seborrheic eczema of both the scalp and the ears.

Medical treatment in this third group varied with the individual patients, depending on the coexisting anorectal disease. Internal hemorrhoids and redundant mucous membrane were treated with injections. Inflamed crypts, fissures and superficially eroded areas were treated with topical applications. For certain painful lesions, as well as for the exaggerated pruritus syndrome, anesthetic oil mixtures were injected subcutaneously for alleviation of the symptoms.

Seborrheic eczema was ignored in this entire series. Nineteen of the patients of the medically treated group had complete relief of their pruritus. Five of these 19 successfully treated patients had recurrences of the pruritus, followed by alleviation of the symptoms on renewing the medical treatment and on eradicating the primary mycotic focus of infection. Four of the remaining medically treated patients were referred elsewhere for completion of their course of treatment.

Of the remaining 22 patients of the entire series, because of complicating cutaneous lesions 2 patients were referred to the other of us (P. D. F.), and those patients are included in the dermatologic series. For the care of the final 20 patients with pruritus ani, a combined surgical and medical program was outlined, 15 patients had active epidermophytosis of the feet, 7 of these patients refused treatment, 11 of the remaining 15 patients responded to treatment with complete alleviation of the symptoms. One of the 11 patients had a recurrence of pruritus, associated with reactivation of mycosis of the feet, and on instituting treatment for the distant foci of infection, the symptoms rapidly disappeared.

In this series of 101 patients, a summary shows that 67 patients had active dermatophytosis, of whom 4 had a combination of seborrheic eczema and a fungous infection of the feet and 6 showed seborrheic eczema alone.

THE TREATMENT OF PRURITUS ANI FOUND MOST EFFECTIVE

The treatment for pruritus ani must depend on the source of the condition as well as on the other complicating factors. Few dermatologists treat only the feet when a well developed dermatophytid of the hands is present. The hands must be treated as well, especially in view of the ever present pruritus. Few proctologists after failing to cure the pruritus by surgical removal of the local pathologic condition consider the associated mycosis of the anus or feet. Therefore, when one is treating pruritus ani in its "id" form, it becomes necessary to treat not only the predisposing cause but also its acute dermatologic manifestations. For that reason, only a very few of our patients were treated for the primary focus alone. In the treatment of pruritus ani, prophylaxis stands out as the first consideration. The following conclusions were drawn largely from the observation of patients with recurrences of the pruritus.

- 1 It is important that patients with pruritus ani should be aware of the necessity of using soap and water, salt water, plain water or a wet cloth, rather than toilet paper. Toilet paper does not thoroughly cleanse the anus, and besides it is rough and irritating, often setting in motion the stimuli which one tries so hard to alleviate.

- 2 It is imperative that the area be kept dry during the day while the patient is up and about. This is often difficult when other anal pathologic conditions are present, such as fissures, hemorrhoids and infected crypts. However, by having men wear suspensories, the amount of perspiration is greatly lessened. It is advisable for women to use an absorbant tampon in the vagina, so that the area is kept as dry as possible from secretions. These expedients, in conjunction with frequent washings and the use of an emollient, will suffice to keep the secondary irritation at a minimum.

- 3 The necessity for removal of all pathologic conditions of the anus which may cause continuation of the symptoms appears to be self evident.

4. The most important part of the entire treatment consists in continuing the therapy for several months after all the symptoms have subsided. Apparently the threshold of resistance of the skin becomes lowered through constant allergic and secondary stimuli. It is necessary, therefore, to continue the treatment to raise this resistance above the point at which cutaneous manifestations will occur.

- 5 Constant attention should be given to seborrheic eczema of the scalp, ear canals, eyelids, axillas or umbilicus, as well as to dermatophytosis of the feet. When these conditions recur, they should be actively treated.

The following therapy has been the most effective in treating our patients and has given better results than any other method heretofore tried (1) a fungicidal ointment, applied to the scalp or the feet or to both, as is indicated by the condition, and applied to the anus at night when no open eczematization exists, (2) vitamin B complex, 200 Sherman units taken twice a day after meals, (3) a diet low in carbohydrate and in fat, (4) roentgen treatment, 75 r weekly, when indicated, (5) medicated dusting powder, applied frequently when the eczematization has subsided

SUMMARY

Of the 145 patients with pruritus ani, 98 had fungous infection of the feet as a complicating factor. Among these patients with a fungous infection, some also had seborrheic eczema. The recurrences following symptomatic cures of the pruritus which were associated with exacerbations of seborrheic eczema and dermatophytosis numbered approximately 50 per cent of the entire series.

The complication of a secondary infection from the common cutaneous contaminants as well as the source of infection from the gastrointestinal tract is of primary importance. It must be kept in mind that the entire length of the anal canal is lined by stratified squamous epithelium which is lacking in its outer horny layer and that most of the fibrous tissue of the reticular layer is also lacking, an increase in permeability being caused as well as a decrease in toughness of the part. Added to these conditions, there is the moisture resulting from the anatomic location of the anus, and it gives a rather complicated picture, which requires intelligent study before an unequivocal diagnosis of the primary source of infection can be made.

It seems that the data presented indicate a definite relationship between seborrheic dermatitis, dermatophytosis and its allergic counterpart, pruritus ani.

CONCLUSIONS

1 There are numerous causes of pruritus ani, local, constitutional and allergic.

2 Pruritus ani is frequently an allergic reaction or "id" resulting from a distant focus of infection, particularly seborrheic eczema or dermatophytosis.

3 In many patients stubborn pruritus ani can be cured only by removing that distant toxic focus.

4 Proper hygiene of the anal and the perianal area must be maintained by all patients with pruritus ani.

FIXED ERUPTION FROM MAGNESIUM HYDROXIDE

POLYSENSITIVITY

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The erythematous pigmentary fixed eruption first reported by Louis Brocq¹ in 1894 was definitely shown to be due to antipyrine. The lesions flared up each time the drug was taken. Since then this type of eruption and others of the urticarial, erythematous and eczematous group, recurring in situ, have been reported following the use of acetophenetidin (phenacetin), acriflavine hydrochloride (trypaflavine), aminopyrine and its compounds, antimony and potassium tartrate, the arsenicals (acetylsan, arsphenamines, mapharsen and triparsamide), barbiturates, bismuth salts, cinchophen (atophan), iodides, ipecac, emetine, ipomea (scammony), isacen (diacetyldihydroxyphenylisatin), mercury, phenolphthalein, quinine and the salicylates (acetylsalicylic acid and sodium salicylate). Other agents, such as vaccines, liquors, psychic stress, physical exertion, menstruation and autotoxic substances, have also been implicated.² Urbach³ reported a fixed eruption from the eating of lentil soup, and Cooke⁴ observed one which followed the eating of tomatoes. Bowen⁵ described a similar eruption from a dental powder containing indian, or karaya, gum, while Loveman and Simon⁶ showed sulfanilamide to be responsible for eruptions also.

Chargin⁷ noted polysensitivity in several persons who presented fixed eruptions due to arsphenamine. The lesions flared up after the

1 Brocq, L. Eruption érythémato-pigmentée fixe due à l'antipyrine, *Ann de dermat et syph* 5 308, 1894

2 Abramowitz, E W, and Noun, M H. Fixed Drug Eruptions, *Arch Dermat & Syph* 35:875 (May) 1937

3 Urbach, E. Ueber fixe nutritiv-allergische Exantheme, *Klin Wchnschr* 15 1208 (Aug 22) 1936

4 Cooke, R A. Personal communication to the authors

5 Bowen, R. Karaya Gum as a Cause of Urticaria, *Arch Dermat & Syph* 39 506 (March) 1939

6 Loveman, A B, and Simon, F A. Fixed Eruption and Stomatitis Due to Sulfanilamide, *Arch Dermat & Syph* 40 29 (Jul) 1939

7 Chargin, L. Fixed Eruption Due to Arsphenamine, *Arch Dermat & Syph* 37:144 (Jan) 1938, Fixed Eruption in a Patient Sensitive to Arsphenamine and Phenolphthalein in Different Areas, *ibid* 38:474 (Sept) 1938

administration of antipyrine, various arsenicals, a bismuth preparation of phenolphthalein, and in 1 case new fixed lesions appeared

In view of these reports, it appears that the cause of a fixed eruption is not limited to a few organic compounds but that any drug may provoke such an eruption. Agents even of a drugless nature may produce such cutaneous manifestations. The explanation that a benzene ring is responsible for a fixed eruption appears inadequate, for bismuth hydroxide and mild mercurous chloride, both inorganic compounds, are known to cause similar lesions²

The following report of a fixed eruption from magnesium hydroxide is interesting, as it shows that first one organic drug and then another and finally a simple inorganic compound caused the same type of eruption in the same patient

REPORT OF A CASE

Mrs M P, a private patient aged 32, was American born, white and the mother of two healthy children. There was no history of allergy. She had always been well except for occasional constipation, for which she obtained relief by taking an emulsion of liquid petrolatum containing agar-agar and phenolphthalein. She never observed any ill effects from its use but discontinued it the latter part of 1938.

The eruption first appeared in 1936, after ingestion of a single dose of phenobarbital, which apparently had been taken for the first time. The cutaneous lesions appeared on the extensor surface of the middle finger and the hypothenar area of the right hand and the little finger of the left hand. They were described as red spots of varying size that left a slight pigmentation. No recurrence developed until 1937, when a rash reappeared in the same areas after the use of the same drug.

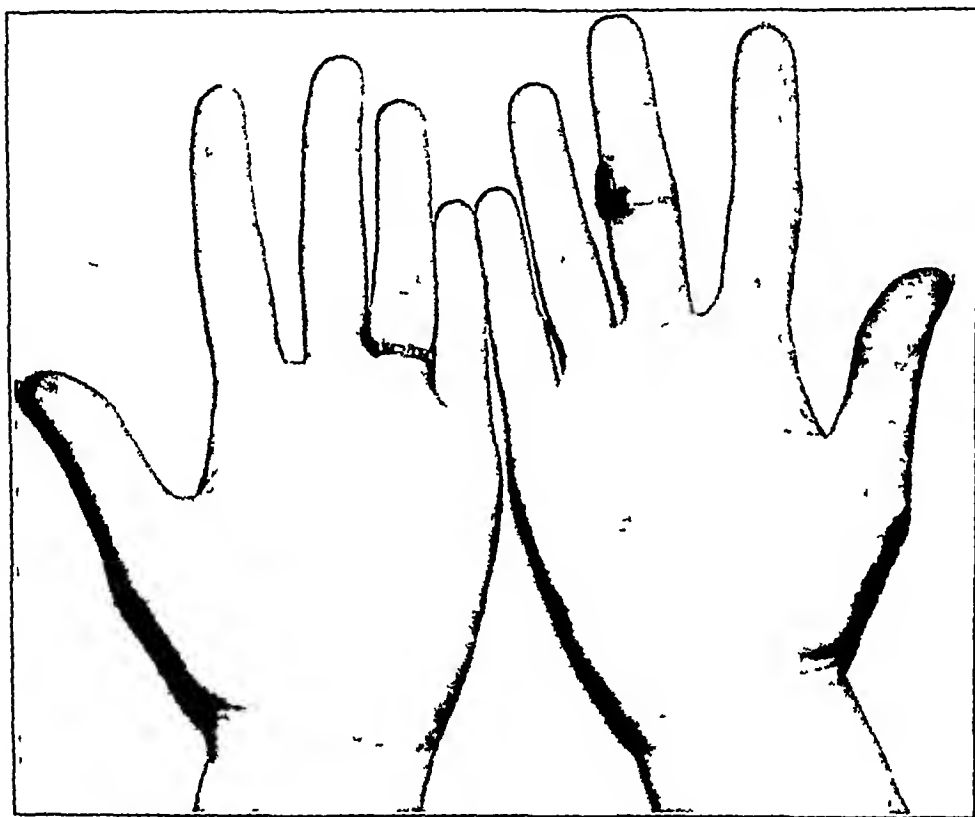
A flare-up of the eruption in the previously involved areas appeared on Feb 12, 1938, after the patient had taken three daily doses of a confectionary tablet containing phenolphthalein. On February 26, when the eruption had subsided, the identical eruption reappeared eight hours after the taking of 1 grain (0.06 Gm) of phenobarbital. No further recurrence developed until December. She then began to use a well known brand of magnesium hydroxide in tablet form, taking 1 tablet daily for seven days. The eruption appeared after the last dose and was similar to the previous outbreaks. The same result occurred later when one of us (J J R) asked the patient to take the tablets of magnesium hydroxide again and also when tablets of another brand of the drug were used.

The patient then avoided all medication until July 22, 1939, when she was directed to take 2 tablets of magnesium hydroxide each day. The recurrence developed about six hours after the last dose on the third day. A similar outbreak developed later, after magnesia magma U S P (suspension of magnesium hydroxide in water) was ingested.

In order to test her sensitivity to other drugs she was given 5 grains (0.32 Gm) of acetylsalicylic acid. One week later she received daily doses of 5 grains (0.32 Gm) of antipyrine, but no reaction developed after ingestion of either drug. During the investigation attention was given to the elimination of anything that might possibly contain phenolphthalein or any other drug. All mouth washes, dentifrices, colored candy, cakes and ice cream were strictly avoided. The makers

of the tablets of magnesium hydroxide, on request, stated that the composition of these tablets was magnesium hydroxide, starch, sugar and oil of peppermint. As the suspension of magnesium hydroxide (magnesia magma) contained none of the ingredients in the tablets except the drug itself, no further testing was done.

The eruption has always been the same, consisting, after the first outbreak of the recurrence in situ, of a circumscribed purplish erythema about the size of a silver dollar located on the hypothenar eminence of the right hand, with a smaller but similarly colored patch on the extensor surface of the middle finger of the right hand and the little finger of the left hand. The eruption is accompanied by itching and usually clears up in two or three weeks, leaving a faint pigmentation. With the taking of the tablets of magnesium hydroxide beginning



Three days after the outbreak of a fixed bullous eruption on the middle finger of the right hand and erythema on the right hypothenar eminence which followed the ingestion of tablets of magnesium hydroxide

on July 22, the patch on the right palm appeared more hemorrhagic, and on the middle finger of the right hand appeared a large bulla. The patient's hands were photographed on July 27, 1939, three days after the outbreak. Consent for a biopsy could not be obtained.

The patient was certain that the eruption never appeared except when she took one dose of phenobarbital, three doses of phenolphthalein or several doses of magnesium hydroxide.

Recurrence in previously affected areas, even though varying from an erythema to a bullous lesion, is characteristic of the so-called "fixed" eruption. The presence of polysensitivity is indicated by the flare-up after ingestion of phenobarbital, phenolphthalein or magnesium hydroxide.

SUMMARY AND CONCLUSIONS

A case is reported in which a fixed eruption followed the ingestion of tablets of magnesium hydroxide, an inorganic substance. The lesions first appeared after the ingestion of phenobarbital, later after that of phenolphthalein and finally after the taking of magnesium hydroxide.

Apparently almost any agent, chemical or otherwise, simple or complex, inorganic or organic, may cause this peculiar manifestation in the skin.

PYODERMA GANGRAENOSUM TREATED WITH SULFANILAMIDE

REPORT OF A CASE

ALFRED L. WEINER, M.D.

CINCINNATI

The association of peculiar recurrent cutaneous ulcers with infectious foci in the viscera was first described as a definite clinical syndrome in 1930 by Brunsting, Goeckerman and O'Leary¹ and was termed by them pyoderma gangraenosum. The authors pointed out that the symptom-complex had probably been described before under a variety of different names and emphasized the striking parallel relation between the activity of the cutaneous lesions and the major infectious focus. Although somewhat rare, the condition has since been reported regularly and consistently enough to justify its consideration as a separate clinical entity.² At the same time some of the confusion in the differentiation of pyoderma gangraenosum from other types of cutaneous gangrene has been overcome. In most of the recorded cases the visceral focus has been in the colon, but other viscera may be involved, as in the case of Lane and Stroud^{2a} (biliary and urinary tracts) and in the case of Weiss, Grollman and Cohen^{2d} (synovial cavities, pleura,

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1 Brunsting, L. A., Goeckerman, W. H., and O'Leary, P. A. Pyoderma (Ecthyma) Gangrenosum. Clinical and Experimental Observations in Five Cases Occurring in Adults, *Arch. Dermat. & Syph.* **22**:655 (Oct.) 1930.

2 (a) Lane, C. W., and Stroud, C. M. Pyoderma Gangrenosum, *Arch. Dermat. & Syph.* **27**:460 (March) 1933. (b) McCarthy, L., and Fields, R. Pyoderma Gangrenosum, *New York State J. Med.* **31**:801 (July 1) 1931. (c) Cohen, M. H. Pyoderma Gangrenosum, *Arch. Dermat. & Syph.* **33**:813 (May) 1936. (d) Weiss, H. B., Grollman, A. I., and Cohen, S. Pyoderma Gangrenosum. Report of a Case with Autopsy, *J. Med.* **18**:239 (July) 1937. (e) Jankelson, I. R., and Massell, B. F. Pyogenic Skin Lesions Accompanying Chronic Ulcerative Colitis. Report of Five Cases, *Am. J. Digest. Dis. & Nutrition* **3**:19 (March) 1936. (f) Gibson, R. Pyoderma Gangrenosa, *Brit. J. Dermat.* **49**:560 (Dec.) 1937. (g) Schmidt, H. W. Hyperimmune Streptococcic Serum in the Treatment of Pyoderma Gangrenosa, Associated with Chronic Ulcerative Colitis and Carcinoma of the Colon, *Proc. Staff Meet., Mayo Clin.* **11**:244 (April 15) 1936. (h) Cowett, M. P. Pyoderma Complicating Ulcerative Colitis, *Am. J. Surg.* **38**:364 (Nov.) 1937. (i) Mintzer, I. J. Pyoderma Gangrenosum, Onychogryphosis and Onycholysis with Ulcerative Colitis, *Arch. Dermat. & Syph.* **40**:541 (Oct.) 1939.

pericardium and urinary tract) Bargaen³ has estimated the incidence of pyoderma gangraenosum in ulcerative colitis as 1 in 1,500 cases

The cutaneous ulcers of pyoderma gangraenosum are characterized by a central area of necrosis surrounded by a purple-blue border beyond which is an erythematous inflammatory areola. There is deep undermining. The crater of the ulcer presents a peculiar gray cribriform appearance. The entire process is further characterized by rapid and extensive sloughing and by slow healing. The resultant scars are smooth, atrophic, cigaret-paper-like and sometimes pigmented and usually assume a serpiginous outline, in the manner of a tertiary syphilid. There is apparently no involvement of the deeper underlying structures. Recurrences as a rule accompany flare-ups in the activity of the associated visceral lesions. Histologically there are necrosis and ulceration, with polymorphonuclear leukocytic reaction in the early acute phase of the lesion and acanthosis, pseudoepitheliomatous epithelial hyperplasia and foreign body reaction in the later stages.¹ Clinically the chronicity, the recurrences, the association of colitis or other systemic disease and the morphologic characteristics of the ulcers of pyoderma gangraenosum serve to differentiate these ulcers from other gangrenous lesions of the skin, such as postoperative gangrene, streptococcic gangrene of Meleney⁴ and dermatitis gangraenosa infantum. Of course, differentiation must also be made from furunculosis or other pyogenic infection of the skin that might occur incidentally during the course of ulcerative colitis, from factitial dermatitis and from other granulomatous lesions, such as bromoderma and blastomycosis, which are not essentially gangrenous.

All observers are agreed that the soil necessary for the occurrence of pyoderma gangraenosum is debilitation caused by some chronic systemic disease. Infection by hemolytic streptococci and staphylococci perhaps in symbiotic relation was advocated as the precipitating cause by Brunsting, Goeckerman and O'Leary.¹ Goeckerman⁵ stated the belief that the cutaneous ulcers were metastatic. Cohen^{2c} considered the entire condition to be a "deficiency disease complex," while Goldman⁶ proposed the attractive theory that the cutaneous ulcers were of the nature of a Schwartzman reaction to the infection in the bowel. Others have seen in pyoderma gangraenosum features suggestive of other types of allergy (e. g., gumma). Engman and Meleney⁷ consid-

3 Bargaen, J. A., in discussion on Schmidt^{2b}

4 Meleney, F. L. Hemolytic Streptococcus Gangrene, Arch Surg 9 317 (Sept) 1924

5 Goeckerman, W. H., in discussion on Lane and Stroud^{2a}

6 Goldman, L., in discussion on Weiss, Grollman and Cohen^{2d}

7 Engman, M. F., Jr., and Meleney, H. E. Amebiasis Cutis (Entamoeba Histolytica), Arch Dermat & Syph 24 1 (July) 1931

ered their cases, presented under the title of amebiasis cutis, to be similar to those of pyoderma gangraenosum even though there was surgical trauma in each of their patients and even though *Endamoeba histolytica* was demonstrated in the visceral and cutaneous lesions in both cases. In a case reported by Guy⁸ there were gangrenous ulcerations of the skin associated with the acute onset of bloody diarrhea. Here nocardia was found to be the etiologic agent. In view of all the varying reports and ideas it seems more reasonable to regard pyoderma gangraenosum as a symptom complex wherein there is underlying constitutional debility and wherein a variety of infectious agents may act as the precipitating cause directly or indirectly.

The treatment of pyoderma gangraenosum is unsatisfactory and in general consists of therapy of the underlying constitutional disorder plus appropriate local applications. Blood transfusions, the administration of serums, vaccines, bacteriophage, arsenic and emetine and a host of local agents have been used. As far as can be determined there are no reports in the literature concerning the use of sulfanilamide for pyoderma gangraenosum. Although the disease is subject to spontaneous remission and exacerbation recovery is exceptional, and in several of the reported cases the condition has proved fatal.

This report is warranted by the relative rarity of reports of cases of pyoderma gangraenosum and by the apparent curative effect of sulfanilamide in the case described herein. Similar encouraging results have been obtained by Collins,⁹ Bannick, Brown and Foster¹⁰ and Brown, Herrick and Barger¹¹ in the treatment of chronic ulcerative colitis with sulfanilamide and its derivatives.

REPORT OF CASE

G. R., a white man aged 31, a steel worker, had been ill since 1932. His illness began with the onset of intractable diarrhea accompanied by a long series of indolent, recurrent cutaneous ulcers. There was some correlation between the number and virulence of the cutaneous lesions and the severity of the diarrhea, but this had not been striking. The typical evolution of an ulceration was as follows: it began as a small vesicle or pustule which rapidly broke down, leaving a deep necrotic area. Surrounding this was a purple-blue halo beyond which was a rapidly advancing erythematous border. There was deep undermining,

8. Guy, W. H. in discussion on Lane and Stroud²¹

9. Collins, E. N. The Use of Sulfanilamide in the Treatment of Chronic Ulcerative Colitis. Preliminary Report of Eleven Cases, *Cleveland Clin Quart* 5:161 1938.

10. Bannick, E. G., Brown, A. E., and Foster, F. P. Therapeutic Effectiveness and Toxicity of Sulfanilamide and Several Related Compounds. Further Clinical Observations. *J. A. M. A.* 111:770 (Aug. 27) 1938.

11. Brown, A. E., Herrick, W. E. and Barger, I. A. Neoprontosil (Oral) in the Treatment of Chronic Ulcerative Colitis, *Proc. Staff Meet. Mayo Clin* 13:561 (Sept. 7) 1938.

sloughing was rapid and extensive, leaving a dirty gray cribriform base. There was no malodor. Healing occurred in from six days to six weeks, depending on the size, site, and extent of a given ulceration, with resultant atrophic, pigmented scars of serpiginous outline. The ulcers varied in size, shape, number and location, but any part of the body could apparently be affected. Trauma seemed to predispose a part to the development of ulceration, on several occasions typical lesions appeared at the sites of the therapeutic injections. Exacerbations for the most part were insidious in onset and usually were unaccompanied with constitutional reaction or flare-up in the activity of the colitis.

The past and family histories were irrelevant. There was no history of syphilis or tuberculosis.

The patient had been hospitalized in various places and for varying periods. Occasionally there had been short remissions of from two to six weeks' duration, when the patient was relatively symptom free. For the most part, however, he had been bedridden for nearly six years. He was under the constant observation

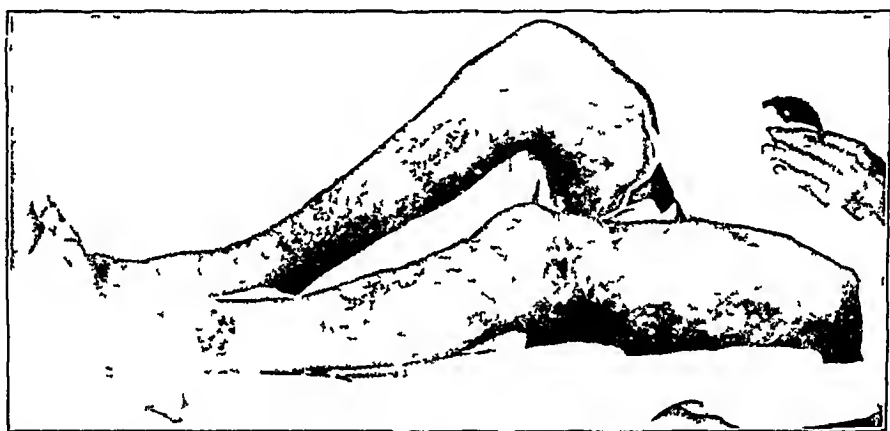


Fig 1—Ulceration of the legs in 1937. Note the depth of the ulcers, the undermining, the cribriform base and the atrophic scarring in healed areas.

of members of the dermatologic staff of the Cincinnati General Hospital from 1936 to 1938 and during this period had rarely been able to leave his hospital bed.

Through the years the gamut of diagnostic and therapeutic procedures had been run. Repeated physical examinations, except for showing the presence of ulcerative colitis, gave negative results. Repeated attempts (including examination on a warm stage) to demonstrate *Endamoeba histolytica* in the lesions of the colon and skin had failed. Examination for blastomycetes and other fungi had given negative results. Hemolytic streptococci were the predominant organisms in the ulcerations of the skin and bowel. There was marked hypochromic anemia. All other laboratory tests gave negative results.

The patient had been subjected to practically every conceivable form of local and systemic treatment, including the transfusion of blood, the administration of antidyenteric and antistreptococcal serums, arsenic (acetarsone), vaccines, calcium and vitamins, and irradiation with ultraviolet and roentgen rays. Various local applications had been used. The result of all treatment was unsatisfactory, although prolonged rest in bed seemed to exert a beneficial effect on the colitis. By the use of occlusive dressings of hard paste of zinc oxide N F (Unna's hard zinc paste) on several occasions, dermatitis artefacta was excluded.

In April 1938 the patient was readmitted to the Cincinnati General Hospital from the Hamilton County Home and Chronic Disease Hospital. At this time several typical large ulcers were present on the back, the right hip and the legs. The patient had been having eight to ten liquid, bloody stools daily. Proctoscopic examination disclosed a picture typical of chronic ulcerative colitis, and hemolytic streptococci, staphylococci and colon bacilli were isolated. The stools contained gross and occult blood, but no amebas or ova were present. Cultures of tissue from the cutaneous ulcerations were negative for amebas and fungi but showed



Fig 2—Healing ulceration of the right leg in 1938

the presence of hemolytic and nonhemolytic streptococci and colon bacilli. Histologic examination of various cutaneous lesions showed extensive areas of necrosis beneath an acanthotic epidermis. Giant cells and other characteristic pathologic changes were absent. No amebas or fungi were present. The arterioles in the subcutis showed a marked intimal proliferation.

Except for anemia, loss of weight and debilitation the results of general physical examination were negative. The red blood cell count was 3,100,000 per cubic millimeter, and the hemoglobin content, 8 Gm per hundred cubic centimeters. The white blood cell count was 8,800 per cubic millimeter, with a normal distribution. Examination of the urine gave negative results, and the Kahn reaction of the blood was negative.

Sulfanilamide was administered on the patient's fourteenth day in the hospital, and approximately 6 to 8 Gm was given daily until a concentration in the blood of 11 mg per hundred cubic centimeters was attained. General supportive measures were instituted, and the patient was given an occasional transfusion of blood. At various times reactions to sulfanilamide, including fever, cyanosis and purpuric eruptions, occurred, and on such occasions it was necessary to discontinue administration of the drug temporarily. It was always possible to resume the giving of sulfanilamide, however, so that a fairly effective concentration of the drug in

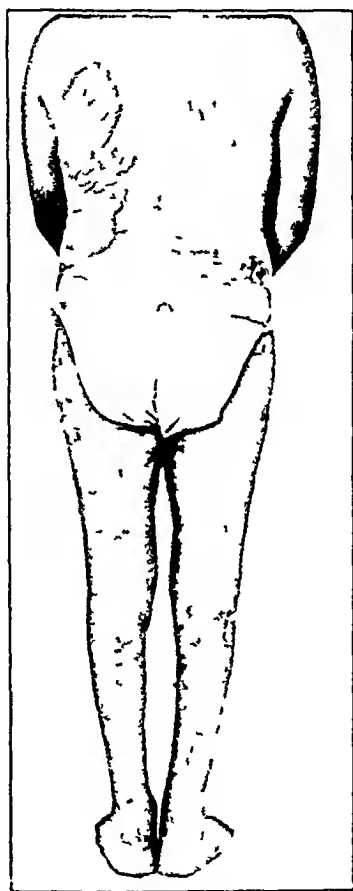


Fig 3—Condition at the time of discharge from the hospital in February 1939. Note the extensive scarring and atrophy of the legs from disuse.

the blood was maintained over a period of several months. During this time the healing of the colitis and of the cutaneous ulcerations was gradual rather than dramatic, and no new lesions appeared as long as the patient received sulfanilamide. It was thought to be significant that on several occasions when the use of the drug was stopped new lesions developed. Over a period of three months the disease was slowly brought under control, the skin was entirely healed, the colitis subsided and the red blood cell count and the hemoglobin content were restored to normal. The patient was able to walk for the first time in more than eighteen months. He gained weight rapidly and was discharged on Nov 26, 1938, after

two hundred and thirteen days of hospitalization. At this time proctoscopic examination showed a great deal of healing in the large bowel, although rare hemolytic streptococci were still present in the stool.

The patient remained in good health and was free of diarrhea and cutaneous lesions for several months, until he suffered a minor bruise of his right thigh, on the site of the trauma a typical serpiginous ulcer developed. There was no recurrence of the colitis or anemia. The patient was readmitted to the hospital, and sulfanilamide was again administered (4 Gm daily) until a concentration of 12 mg per hundred cubic centimeters of blood was reached. The ulcer healed within two weeks, and the patient was discharged on Feb 15, 1939. Since that time he has been carefully observed in the dispensary and given occasional small amounts of sulfanilamide. At the time of writing there has been no recurrence of the colitis or of the cutaneous lesions. A recent proctoscopic examination showed much scarring but no ulcerations in the large bowel.

SUMMARY AND CONCLUSIONS

A patient with pyoderma gangraenosum of six years' duration was successfully treated with sulfanilamide.

The pertinent literature is reviewed, and the opinion is expressed that pyoderma gangraenosum is a symptom complex with which there is underlying constitutional debility and various infections may act directly or indirectly as the exciting cause.

NOTE—The patient was recently (Feb 5, 1940) observed and studied. There has been no recurrence of any of the symptoms.

615 Union Central Building

QUALITATIVE MEASUREMENTS OF LOW VOLTAGE SHOCK-PROOF X-RAY TUBES

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BUFFALO, N Y

The recent introduction by the manufacturers of low voltage x-ray therapy tubes which are both ray proof and shock proof offers the roentgenologist or the dermatologist certain advantages, such as safety from electrical shock and the ability to treat at shorter distances, and opens the field of intracavitary irradiation. On the other hand, there is the disadvantage that with such equipment the inherent filtration is considerably greater than with the older type of x-ray tubes with thin glass walls.

The question is immediately raised. Can such shock-proof equipment meet the requirements for therapy with low voltage, unfiltered radiation, or, in other words, does the inherent filter in the new tube produce a beam which is harder than that usually used for superficial therapy?

It is well known, particularly with mechanical rectification and thin-walled x-ray tubes, that the qualitative agreement among various machines operating at the same voltage and current and having the same filtration is poor. For instance, one generator and tube operating at 120 kilovolts peak may deliver a "softer" radiation than another combination operated at 80 kilovolts peak. The use of valves in rectification has improved the situation, but there may still be a wide variation between two different installations.

There is, however, the possibility that the values of the new shock-proof tube would fall within the extreme qualitative limits of the older equipment. Therefore, a study was made of the quality of the x-ray beams emitted through thin-walled tubes by approximately twenty generators, with rectification either mechanical or by valves. The data have been assembled during the past ten years, as a result of calibration of various installations for superficial therapy. The generators were operated at 70 and 100 kilovolts peak, with no filter or with 1, 2 or 3 mm of aluminum. The results of the study are shown in charts 1 and 2. The quality of the radiation is expressed as effective wavelength, and the values for all the machines operated at 70 kilovolts peak

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fall within the shaded area of chart 1. Similarly the shaded area of chart 2 represents the qualitative distribution of all generators and tubes operated at 100 kilovolts peak.

It is interesting to note, when comparing chart 1 with chart 2, that there is considerable overlapping of the two sets of values. In other words, as already mentioned, some generators produced rays at 100 kilovolts peak which were softer than those produced by other machines at 70 kilovolts peak.

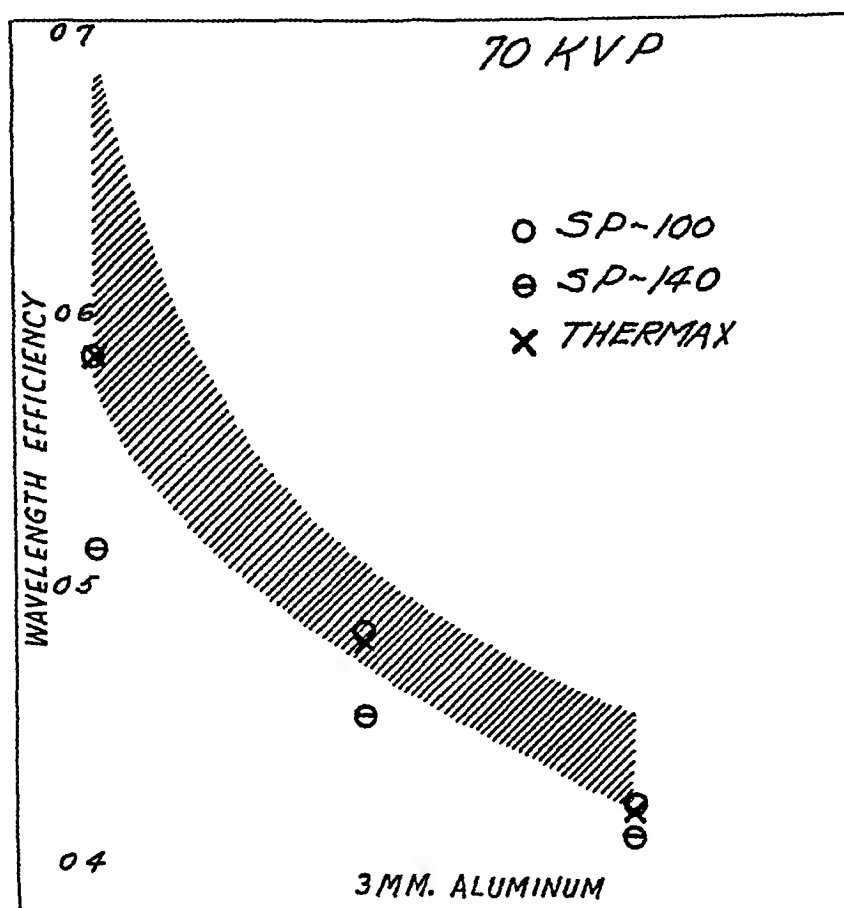


Fig 1—Quality of rays emitted by various x-ray tubes at 70 kilovolts peak. The shaded section shows the range of qualities for twenty x-ray tubes with thin glass walls, O, ⊖ and X are the average qualitative values for oil-immersed shock-proof x-ray tubes.

While it is true that the manufacturer gives the equivalent inherent filtration for the new equipment, it should be emphasized that equivalence is frequently quantitative only and that this inherent filter does not necessarily produce the same hardening effect as that produced by the same thickness of the metal when used as a filter. The average qualitative values are therefore presented and represent measurements made at calibrations of some of the newer shock-proof tubes. The calibra-

tions were made with the SP 100, SP 140 and the XPT tubes of the General Electric X-Ray Corporation and with the thermax tube of the Machlett Laboratories. The effective wavelengths were determined by measuring the absorption of rays by 1 mm of aluminum and are indi-

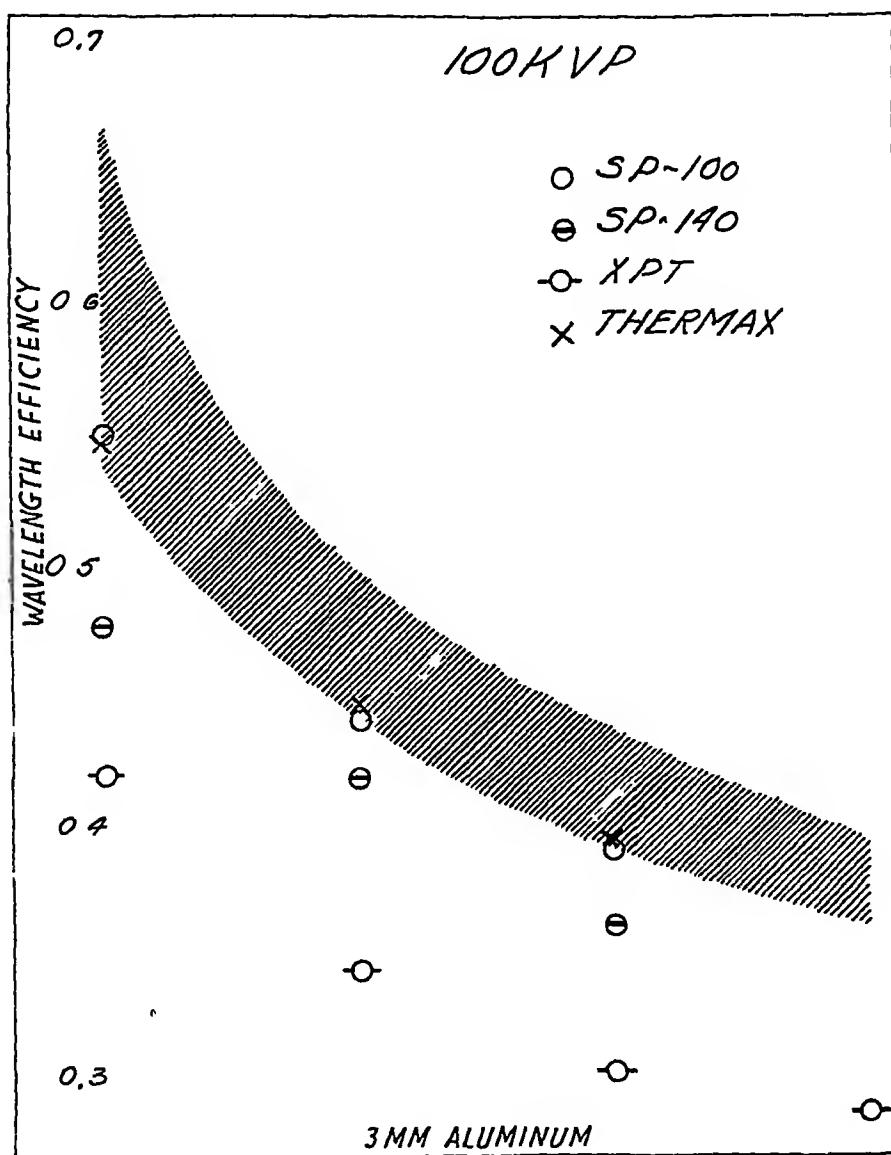


Fig 2—Quality of rays emitted by various x-ray tubes at 100 kilovolts peak. The shaded section shows the range of qualities for twenty x-ray tubes with thin glass walls, O, ⊗ and X are the average qualitative values for oil-immersed shock-proof x-ray tubes.

cated on charts 1 and 2 for the same voltages. It is evident that with certain of the shock-proof tubes the qualitative expectancy is close to the lower (or short wavelength) border of the qualitative expectancy

of tubes of the older type. In no instance are the values for the new tubes comparable to the average values obtained from the old thin-walled tubes. The values for other shock-proof tubes fall definitely beyond the short wavelength range of the thin-walled tubes and can be compared only with the filtered radiation of the older type tubes.

For purposes of comparison, the qualitative data obtained from an XPT tube operated at 100 kilovolts peak are included in chart 2.

SUMMARY

Qualitative measurements of x-rays made with the new shock-proof tubes designed for superficial therapy at low voltage are compared with the measurements made with twenty installations in which a thin-walled x-ray tube was used.

RETICULUM CELL SARCOMA

REPORT OF A CASE WITH PRONOUNCED CUTANEOUS MANIFESTATIONS

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AND

S S QUARRIER, M D

HARTFORD, CONN

Multiple tumor nodules in the skin have been reported as occurring in the course of many malignant diseases. Almost every type of epithelioma, sarcoma or lymphoma has been known to involve the skin secondarily, but only a few types, such as melanoma, leukemia, Hodgkin's disease and cancer of the breast and of the stomach have given widespread cutaneous metastases. As such cutaneous involvement is uncommon, we are reporting a case of reticulum cell sarcoma in which the cutaneous manifestations were the outstanding clinical feature.

In considering the differential diagnosis in the case which follows, Recklinghausen's disease, with countless neurofibromatous nodules scattered diffusely over the body, comes first to mind, but the sudden onset and the rapidly fatal course exclude this at once. Generalized lymphadenopathy is strong presumptive evidence of lymphoma as opposed to carcinoma and sarcoma, while a lack of pigmentation is against melanoma. A superficial examination serves to exclude all other multiple tumors primary in the skin.

REPORT OF CASE

History—A 56 year old married American textile worker was well until June 1, 1937, when he noticed a lump under his jaw. Two weeks later he began to notice general malaise, weakness, constipation with ribbon-like stools, swelling of the glands in the groin and nodules in the skin. The nodules and glandular swellings increased from this time on in number and in size until his death on August 19, two and one-half months after their appearance. His course was gradually downhill, with increasing weakness, loss of weight, dyspnea and cyanosis. He was given a course of high voltage roentgen ray therapy but without change in his general condition. Death was the result of respiratory failure with circulatory collapse.

Past History—The patient had been in the Hartford Hospital in September 1927, ten years before the onset of his present illness. At that time a diagnosis of general peritonitis with pelvic abscesses was made, and the patient underwent three operations. On admission a laparotomy was performed, and several pockets of

From the departments of Medicine and Pathology of the Hartford Hospital

pus were drained. The appendix could not be found. An ileostomy was done, and the opening was kept open for a month. The first attempt at closure was unsuccessful, but a month later the fistulous tract was excised, a piece of calcified tissue was extracted and healing occurred. The patient's entire course in the hospital was stormy, but he was discharged in good condition. Physical examination at that time showed no abnormal lymph glands or cutaneous nodules. On admission the leukocyte count was 16,000 per cubic millimeter, with a differential count of 91 per cent neutrophils.

On June 21, 1937, the patient was admitted to the Hartford Hospital for the second time, in the surgical service of Dr Alfred M Rowley, for removal of a cutaneous nodule for biopsy. The man appeared fairly well developed and well nourished but chronically ill. The skin over the chest, abdomen and thighs contained many nodules of varying size up to 2 cm in diameter. The nodules were firm, nontender and intracutaneous but freely movable over the underlying tissues. A few were pink, but most showed no discoloration of the overlying skin. The

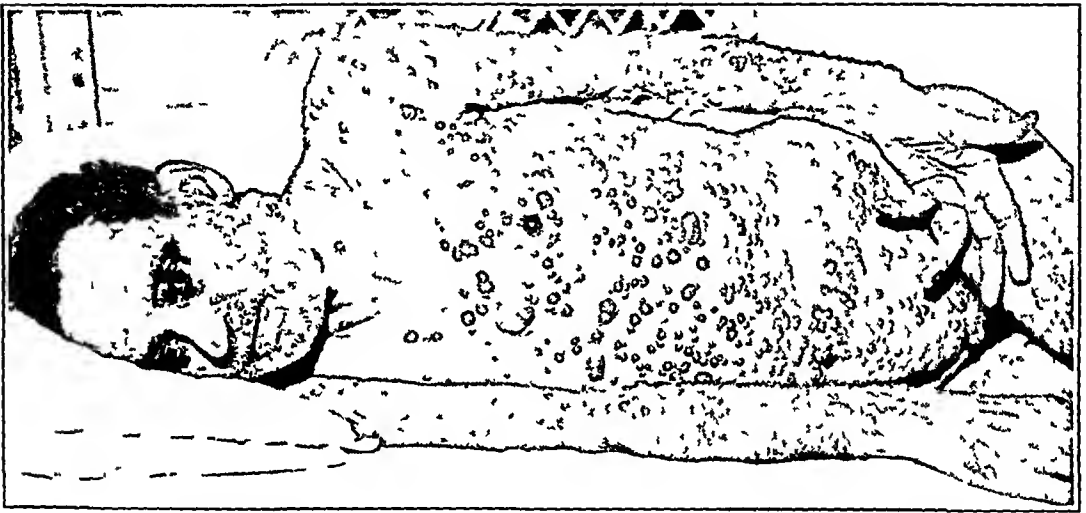


Fig 1—A patient with reticulum cell sarcoma, three days before death

eyes, nose and ears were normal. The mouth showed evidence of poor hygiene with dental caries, pyorrhea and an enlarged, red, grossly infected right tonsil with purulent exudate at the crypt openings. The cervical, axillary and inguinal nodes were enlarged bilaterally. They were firm, slightly tender and partially fixed to the underlying tissue. The chest was clear and the heart sounds normal. The blood pressure was 138 systolic and 75 diastolic. The abdomen was normal except for an old scar in the right lower quadrant and a small incisional hernia. The spleen and liver were not felt. The extremities, thyroid gland, breasts, skeleton, reflexes, rectum, and genitalia appeared normal.

Two months later, on August 14 the patient was admitted to the Hartford Hospital for the third and last time, this time in the medical service of Dr Orin R Witter. Emaciation, weakness and dyspnea were pronounced. Many more cutaneous nodules had appeared, and they now covered the arms, scalp and face (fig 1). The right tonsil was more inflamed and swollen, lymphadenopathy was more pronounced, and signs of gross hydrothorax were present on the right side. Examination of the heart revealed a few dropped beats, and the blood pressure had fallen to 110 systolic and 90 diastolic. The liver was enlarged and palpable at the level of the umbilicus, but the spleen was never felt.

Laboratory Observations—In June the hemoglobin content was 81 per cent (126 Gm per hundred cubic centimeters), the red blood cell count was 5,000,000 and the white count, 13,400 per cubic millimeter, with a differential count of 83 per cent neutrophils, 14 per cent lymphocytes and 3 per cent monocytes. No abnormal cells were found in the blood smear. Two months later and just before death the hemoglobin was 82 per cent, and a blood smear showed no abnormality other than 87 per cent neutrophils in the differential count. Three urinalyses gave negative results. The Wassermann reaction of the blood was negative. Clear yellow pleural fluid (1,500 cc) removed from the right side of the chest was sterile on culture, contained 20 Gm of protein per liter and had a specific gravity of 1.014 and a cell count of 1,800 per cubic millimeter, of which 400 cells were white blood cells, 27 per cent of these being neutrophils and the remainder monocytes. Further examination of the sediment showed no diagnostic tumor cells but a



Fig 2—Section of lung showing extensive peribronchial infiltration

few round cells and plasma cells. A culture of material from the right tonsil showed a 4 plus mixed flora without Vincent's bacilli. Roentgenograms of the chest three days before death and just after thoracentesis showed signs of consolidation at the base of the right lung suggestive of atelectasis with associated fluid. The diagnosis based on the biopsy of a cutaneous tumor was reticulum cell sarcoma of the skin.

Observations at Autopsy—The skin of the face, neck, chest, abdomen, back, arms and to a lesser extent thighs was studded with firm elevated nodules varying up to 3 cm in size. The nodules were skin colored, red or nonpigmented, and the overlying epidermis was tensely stretched, giving a glistening appearance. Cut sections of the nodules showed firm grayish white tissue covered by a thin layer of epidermis, suggesting an intracutaneous position. The cervical, axillary and inguinal lymph glands were decidedly enlarged, some measuring 6 cm in diameter.

On the visceral pericardium were several tumor nodules measuring 1 cm. There was 1,500 cc of slightly bloody fluid in the right pleural cavity and 200 cc

in the left. On the pleural surfaces of both lungs, more so on the right, were several firm tumor nodules measuring 1 cm. The bronchial mucosa appeared diffusely thickened but not ulcerated or nodular. Even the tertiary branches stood out from the parenchyma of the lung as rings of white cellular tissue (fig 2). The gastrointestinal tract showed no pathologic changes except for old fibrous adhesions between the terminal portion of the ileum, the cecum and the abdominal

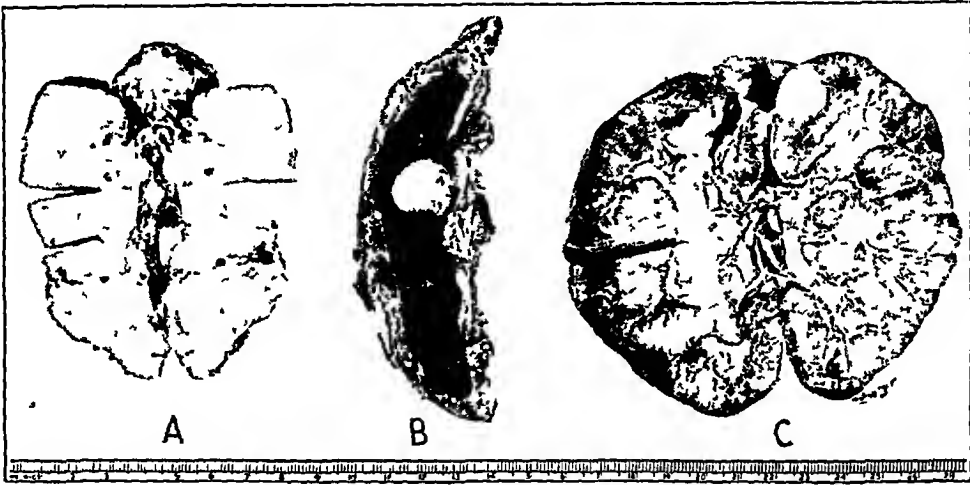


Fig 3—*A*, section through mass of retroperitoneal lymph glands replaced by tumor tissue. *B*, section of spleen with nodule of tumor tissue. *C*, section of kidney showing single nodule of tumor tissue.



Fig 4—Section through liver showing multiple nodules of tumor tissue, many of them appearing black in the photograph due to hemorrhage.

scar. The appendix was not seen. The spleen weighed 140 Gm, and a cut section revealed a 3 cm white tumor nodule in the mid portion. There was no gross hypertrophy of the malpighian corpuscles (fig 3*B*). The pancreas showed considerable compression due to massive enlargement of the adjacent lymph glands. The liver weighed 2,800 Gm. The capsule presented a coarsely nodular surface. A cut section revealed many tumor nodules throughout the parenchyma (fig 4), some of which were soft and showed hemorrhagic degeneration. The gallbladder

contained many small cholesterol stones, and the wall was slightly thickened. The ducts were clear. In the cortex of the right adrenal gland was an 8 mm yellowish encapsulated tumor. In the upper pole of the right kidney was a 2 cm white nodule which was not at all encapsulated but faded off gradually into the normal parenchyma (fig 3C). The pancreatic, periportal, aortic and iliac nodes showed a massive enlargement and were composed of moderately firm homogeneous grayish white tissue, with some areas of interstitial hemorrhage (fig 3A). The bladder, genitalia, skeleton, bone marrow and brain showed no gross pathologic changes.

Microscopic Observations—Sections through several of the enlarged lymph glands showed a complete absence of the normal follicular arrangement and in its

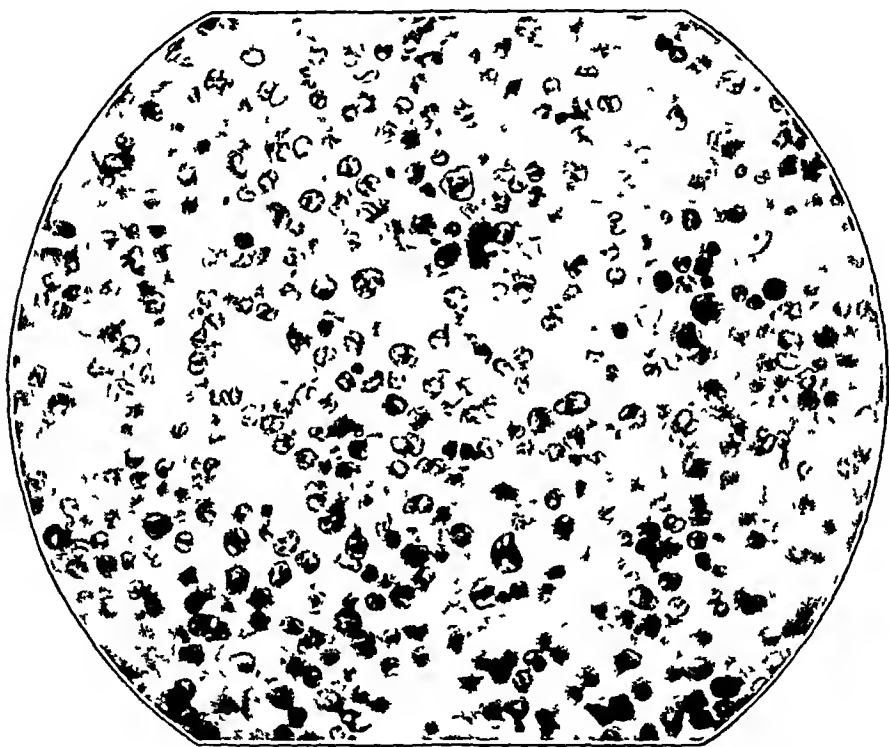


Fig 5—Lymph node showing characteristic type cell ($\times 320$)

place a homogeneous cellular tissue composed of anaplastic cells, with large vesicular nuclei and a small, often indefinite, amount of eosinophilic cytoplasm. In general, the nuclei had an oval shape, however, crescentic, lobulated and even multiple forms were not uncommon, and some of the latter suggested Sternberg-Reed cells (fig 5). The nucleoli were inconspicuous. Mitosis occurred frequently, there were often as many as ten to fifteen dividing cells in a high power field. Little stroma was present, capsular infiltration was slight, and eosinophils and lymphocytes were scarce, but necrosis of the infarction type was rather pronounced.

The cutaneous nodules were composed of similar neoplastic cells, which lay in masses in the corium and were covered with a thin layer of squamous epithelium. The nodules were not encapsulated but invaded the subcutaneous and muscle tissues in places. The pericardial metastases, which in one place had actually

invaded the cardiac muscle, had similar cytologic structure. There were numerous metastatic nodules throughout the lungs, most of which were on the pleural surface but some of which were seen deep in the parenchyma of the lungs surrounding small lymphatics. Sections through the bronchi revealed a striking submucosal infiltration with tumor cells (fig 6). The epithelium was intact and showed no hyperplasia. The spleen, liver and kidneys showed similar metastatic involvement. The normal marrow of a vertebral body had been largely replaced by neoplastic cells. In the right adrenal was a small cortical adenoma.

Anatomic Diagnoses—The anatomic diagnoses were (1) reticulum cell sarcoma, with involvement of the lymph glands, skin, pericardium, lung, bronchi,



Fig 6—Bronchus showing submucosal tumor infiltration ($\times 84$)

spleen, liver, kidneys and bone marrow, (2) chronic cholecystitis, with cholelithiasis, and (3) cortical adenoma of the adrenal.

COMMENT

The condition in the case presented was undoubtedly a lymphoma of the sarcomatous type, with diffuse metastases and local invasive tendencies. The more exact name reticulum cell sarcoma seems justifiable in view of the morphologic appearance of the cells, the normal blood picture and the lack of many characteristic Hodgkin giant cells. Aleukemic reticulosis and Hodgkin's sarcoma are the only other possible diagnoses, and in our opinion they are merely other names for practically identical conditions.

In line with the work of Jackson¹ and Parker² at the Boston City Hospital we have used type cell morphology as the basis of differentiating members of the lymphoma series

SUMMARY

A case of rapidly fatal reticulum cell sarcoma has been presented because of the unusually pronounced cutaneous manifestations

751 Asylum Avenue

1 Jackson, H, Jr Classification and Prognosis of Hodgkin's Disease and Allied Disorders, Surg, Gynec & Obst 64 465, 1937

2 Parker, F, Jr Personal communication to the authors

CUTANEOUS HYPERSENSITIVITY TO TRIETHANOLAMINE

REPORT OF TWO CASES

GEORGE H CURTIS, MD

AND

E W NETHERTON, MD

CLEVELAND

Triethanolamine is extensively used in the manufacture of cosmetics and in dermatologic therapy Maynard¹ has pointed out the value of its emulsifying and skin-softening properties when used in ointments and oily bases to facilitate their removal from hairy surfaces and to increase the penetration of medicaments into the skin Goodman² has indicated its extensive use in the manufacture of soap and cosmetic cream Commercial triethanolamine, consisting of 2 to 5 per cent monoethanolamine, 11 to 20 per cent diethanolamine and over 80 per cent triethanolamine, is as efficacious as triethanolamine of 99 per cent purity

In view of the wide use of the chemical by manufacturers and its increasing use in dermatologic therapy, it is to be expected that some cases of cutaneous hypersensitivity of the contact eczematous type will occur, although Goodman^{2a} has applied triethanolamine to denuded cutaneous surfaces without producing irritating symptoms Maynard and Goodman emphasized the fact that in their experience triethanolamine has not irritated the skin even in concentrations as high as 15 per cent A manufacturer³ also stated that the chemical has not been known to irritate the skin In view of these facts and because we have been unable to find in the literature any reference to irritation of the skin due to triethanolamine, the following 2 cases of cutaneous hypersensitivity to triethanolamine are reported

From the Cleveland Clinic Foundation Hospital

1 Maynard, M T R Triethanolamine Adjunct to Dermatologic Therapy, *Arch Dermat & Syph* 25:1041-1045 (June) 1932, Triethanolamine Adjunct to Dermatologic Therapy, with Special Reference to Ringworm of the Scalp, *ibid* 34 268-270 (Aug) 1936

2 Goodman, H (a) Triethanolamine, *Am Perfumer*, May 1936, (b) *Cosmetic Dermatology*, ed 1, New York, McGraw-Hill Book Company, 1936

3 American Carbide and Chemicals Corporation (information given in personal communications by Dr H F Smith Jr and Mr H B McClure)

CASE 1—A white man aged 45 came to the clinic on May 3, 1937, complaining of a dermatitis on the face, neck and upper part of the chest of one week's duration. The dermatitis appeared suddenly with burning and itching.

The results of general physical and laboratory examinations were normal. The skin of the face, the anterior aspect of the neck and the upper part of the chest was red and swollen and showed much weeping, crusting and vesiculation.

A tentative diagnosis of contact dermatitis was made, and careful questioning narrowed the possible irritants down to nose drops of metaphen with epinephrine (metaephedrine), a hair tonic and a brushless shaving cream. Patch tests with the nose drops and the hair tonic gave negative results, while the site of the test with the shaving cream showed a strong positive reaction. It was not possible to test with the separate ingredients of the shaving cream, but it was found that the cream contained triethanolamine. Patch tests with 1 to 1,000, 1 to 1,500 and 1 to 100 aqueous dilutions of triethanolamine applied some months after the dermatitis subsided gave strongly positive results, and, in addition, produced a flare-up of the dermatitis on the cutaneous surfaces previously affected.

CASE 2—A white woman aged 41 came to the clinic on Nov 4, 1937, complaining of dandruff and a recurrent dermatitis of nine months' duration along the hair line of the scalp and on the ears.

The results of general physical and laboratory examinations were essentially normal. The scalp showed a moderate amount of dandruff and typical plaques of seborrheic eczema along the hair line. The ears showed typical seborrheic eczema and fissures at their bases.

An ointment consisting of 2 per cent salicylic acid, 4 per cent sulfur precipitate, 3 per cent resorcinol and 4 per cent triethanolamine in an oxycholesterol-petrolatum base was prescribed. At the end of three weeks the scalp was free of the dandruff and dermatitis, but the ears showed some scaling, and a small fissure behind one ear still remained. The patient complained of a slight itching in the ears. A lotion was substituted in place of the ointment for the scalp, while the ointment was applied to the ears. Two days later she returned with a marked eczematous dermatitis on the face, including the eyelids, and on the ears, neck and upper part of the chest and arms. The scalp showed no dermatitis.

After the dermatitis subsided, patch tests with the ingredients of the ointment were applied. The sites tested with salicylic acid and sulfur showed no reaction, while the sites tested with 1 to 200 and 1 to 100 dilutions each of triethanolamine and resorcinol gave strongly positive reactions. The patient refused to allow further studies to be made, but after the dermatitis subsided she continued to use salicylic acid and sulfur in ointment form with satisfactory results.

In the first case, although it was not possible to test the separate ingredients of the shaving cream, the facts that the cream contained triethanolamine and that patch tests with dilute solutions of the chemical produced strong positive reactions and a flare-up of the dermatitis on previously affected cutaneous surfaces seem to be sufficient proof that triethanolamine caused the dermatitis. In the second case it was not possible to make more detailed studies in order to determine what part triethanolamine played in producing the dermatitis. However, the sites of the patch tests with 1 to 200 and 1 to 100 dilutions of the

chemical showed strong eczematous reactions, which in themselves are sufficient proof that the patient's skin became hypersensitive to triethanolamine

Since the discovery of these 2 cases we have made one hundred patch tests to date on as many persons and have not obtained a positive

Patch Tests with Various Dilutions of Triethanolamine*

| Number of Tests | Dilution | Number of Reactions |
|-----------------|--------------------|---------------------|
| 16 | 1 100 (1 per cent) | 0 |
| 35 | 1 20 (5 per cent) | 0 |
| 13 | 1 10 (10 per cent) | 0 |
| 26 | Undiluted | 0† |

* The materials for testing were applied for forty eight hours, and the skin was observed for ninety six hours

† Two test sites showed a number of pinhead sized erythematous papules which disappeared in a few days, leaving a slight shiny wrinkled scale, such as is seen when dilute soap or sodium and potassium hydroxide solutions are applied to the skin. These test sites were not considered positive

reaction (table). Thus, if some reliance can be placed on this small number of tests and on the experience of Maynard and Goodman, it is safe to assume that cutaneous hypersensitivity to triethanolamine is rare.

GENERALIZED TRICHOPHYTON PURPUREUM INFECTION SIMULATING DERMATITIS HERPETIFORMIS

REPORT OF A CASE

JESSE A TOLMACH, M D

AND

JOEL SCHWEIG, M D

NEW YORK

We have recently observed a case of unusual and extensive infection of the skin due to *Trichophyton purpureum*. Until the causation was conclusively proved, dermatitis herpetiformis was considered a most probable diagnosis by a number of competent observers.

REPORT OF CASE

History—A F, a Jew aged 38, was born in Hungary and had been in the United States about fifteen months. He was a traveling dry goods salesman, was married and had two children. No other member of his family was known to have had any cutaneous eruption. He was enjoying good health until his present illness. In 1938 he underwent a tonsillectomy. He has had bleeding hemorrhoids for the past two or three years.

His present illness began in 1934, while he was traveling and sleeping in unsanitary surroundings. The eruption first appeared on his thighs and back and then spread to other parts of his body. He was under constant medical care abroad and in the United States without ever getting well. In 1937 he was hospitalized in Vienna, Austria, where treatment was given with roentgen and ultra-violet radiation, lotions, pastes and vaccines. All these remedies gave only temporary relief. His chief complaint was the unbearable itching, which could be relieved only by severe excoriations with his nails or with a sharp instrument. He did not take laxatives, headache powders or any other drugs. During his illness, which has lasted about six years, there has never been a period of more than two weeks of complete freedom from the eruption.

Physical Examination—The patient was a well proportioned and well built, slightly obese man. Except for his cutaneous lesions and several lipomas on his arms and hips, nothing abnormal was found.

The dermatosis involved almost two thirds of the entire integument. The only unaffected areas have been the face with the exception of the forehead, the flexor

From the Department of Dermatology and Syphilology, Beth Israel Hospital, service of Dr. Oscar L. Levin.

The case was presented in May 1939 before the Section of Dermatology and Syphilis of the New York Academy of Medicine (ARCH DERMAT & SYPH 40 1057 (Dec) 1939).

surfaces of the arms, the flanks, the hands and the lumbar region. The mucous membrane of the mouth was also unaffected. The affected areas presented large dull red patches with sharply margined borders. The marginal lesions were made up of papules and vesicles, most of them excoriated and arranged in a serpiginous line producing bizarre figures. There were also scattered groups of papulovesicular lesions within the patches. The occasional scaling present was fine, thin and adherent to the underlying skin. The removal of the scales caused a slight amount of bleeding. The lesions in the armpits and groins and on the toes were macerated and moist and gave off an offensive odor. The nails of the hands and feet were free. None of the patches showed a tendency to clearing in the center, the only difference between the central and the marginal lesions being in the degree of induration. The itching was intense, and the patient constantly scratched himself. During the period of observation, which extended over eleven months, the clinical picture changed almost kaleidoscopically. Large patches would break up into small groups or clusters made up of excoriated papular and papulovesicular lesions. Previously affected areas would clear temporarily, and new regions would be invaded. The changes were accompanied by the most intense and intolerable itching.

Laboratory Observations—The Wassermann reaction was negative. Urinalysis gave negative results. The blood count revealed no abnormality. Repeated examinations of the scales from the lesions on the abdomen, axillae, back, groins and forehead revealed the presence of fungi. Cultures from these areas showed *T. purpureum*. Trichophytin tests with dilutions of 1 to 10 and 1 to 30 were negative after forty-eight hours, as was the oidiomycin test.

The histologic examination showed a simple inflammatory process involving the upper part of the cutis and the epidermis.

The patient responded favorably to applications of fungicidal preparations, such as compound ointment of benzoic acid N F (Whitfield's ointment) and dilute tincture of iodine. Recurrences appeared soon after discontinuance of the medication.

COMMENT

Cases of extensive involvement of the cutaneous surface as a result of *T. purpureum* infection have been reported, but they are uncommon. Payenneville and Rivalier¹ studied a case of an extensive and bizarre infection with *Trichophyton rubrum*. The latter organism is the same as *T. purpureum*. Bang² described *T. purpureum* infection involving the arms and the abdomen. Recently Lewis, Montgomery and Hopper³ made a valuable contribution to the knowledge of cutaneous manifestations of infection with *T. purpureum*. They observed in 3 instances

1 Payenneville, J., and Rivalier, E. Un cas d'épidermophytie exotique, *Ann de dermat et syph* 8:378 (May) 1937.

2 Bang, H. Sur une trichophytie cutanée à grands cercles, causée par un dermatophyte nouveau (*Trichophyton purpureum* Bang), *Ann de dermat et syph* 1:225 (May) 1910.

3 Lewis, G. M., Montgomery, R. M., and Hopper, M. E. Cutaneous Manifestations of *Trichophyton Purpureum* (Bang), *Arch Dermat & Syph* 37:823 (May) 1938.

eruptions involving large areas of the skin of the trunk. They further stated that the various clinical manifestations may simulate psoriasis, arsenical keratosis, neurodermatitis, eczema, sycosis vulgaris and erythema annulare centrifugum (Daiier)

In referring to *T. purpureum* infections of the glabrous skin, Lewis, Montgomery and Hopper stated that there is rarely any noticeable vesiculation. In our case, vesiculation was an obvious feature of the



Fig 1—Distribution of the eruption. Note the clusters of vesicular lesions above and below the operative scar and on the thigh.

eruption when the patient was first observed by us. Subsequently, only occasional vesiculation was noted.

The presence of vesicular and papulovesicular lesions, the distribution of the eruption, the chronicity and the intense itching in this case gave a distinct impression of dermatitis herpetiformis (figs 1 and 2). In fact, this diagnosis was made by a number of competent dermatologists before the mycologic studies were completed.

The possibility of the eruption's being an extensive eczematous dermatophytid as a consequence of tinea cruris was ruled out by the finding of *T. purpureum* in all the affected parts. Further evidence against the possibility of diagnosing the condition in this case as a dermatophytid lay in the presence of negative trichophytin reactions after forty-eight hours. Negative or only slightly positive reactions to trichophytin are the rule in *T. purpureum* infections.

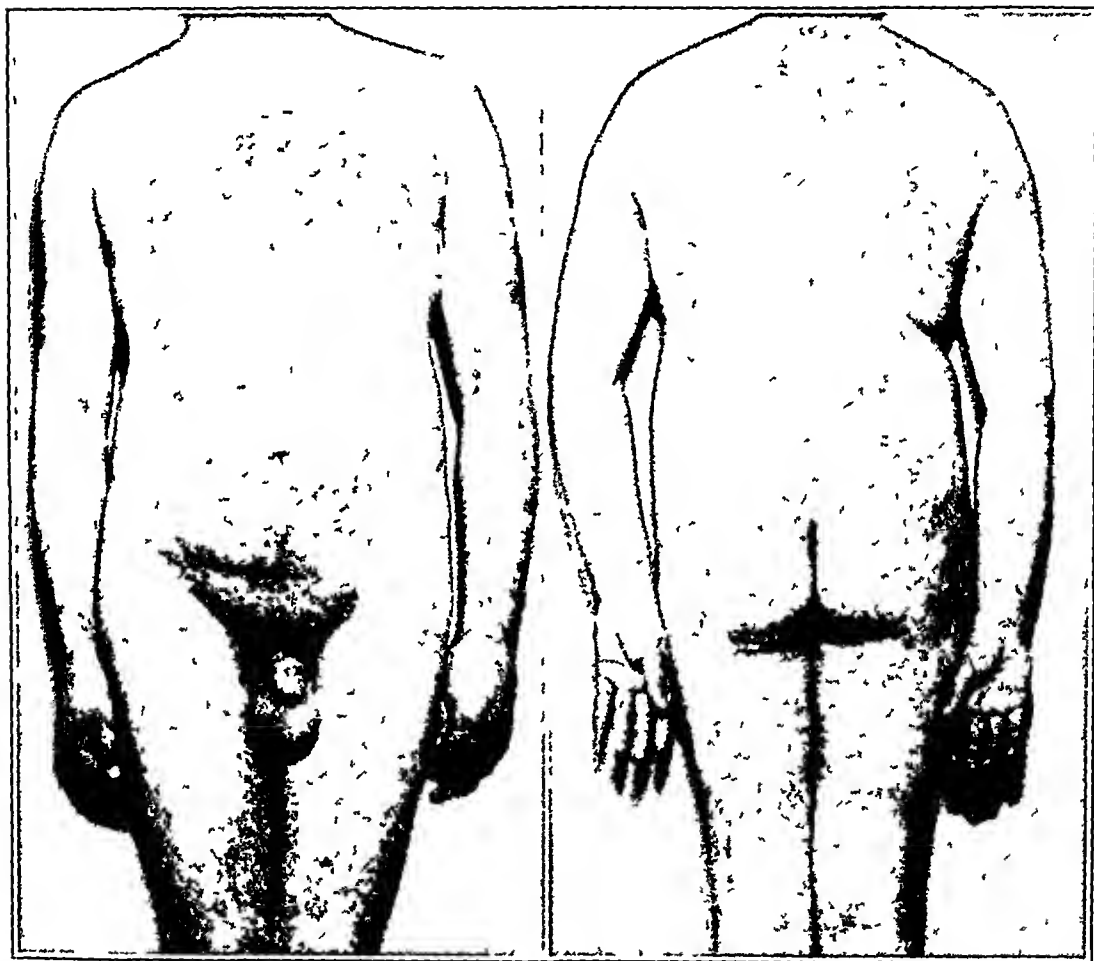


Fig 2—Distribution of the eruption. The area surrounding the umbilicus cleared after applications of compound ointment of benzoic acid N F. Note the tendency toward grouping. The palms show no evidence of the eruption.

SUMMARY

An extensive and bizarre infection with *T. purpureum* is reported. Its appearance closely resembled that of dermatitis herpetiformis. The value of careful mycologic investigation is obvious.

30 West Fifty-Ninth Street

47 East Sixty-First Street

Clinical Notes

USE OF UREA (CARBAMIDE) IN TREATMENT OF WARTS (VERRUCA VULGARIS)

EATON M. MACKAY, M.D., LA JOLLA, CALIF

The observation that strong aqueous solutions of urea (carbamide) possess considerable virucidal power in so far as the agents responsible for rabies and poliomyelitis are concerned¹ led me to examine the possibility that they might be useful in the treatment of common warts (verruca vulgaris). These lesions may be transmitted by a sterile filtrate of wart material and are presumably due to a filtrable virus.² When attempting to make virus vaccines with the aid of urea,¹ I observed that urea "solutions" of human warts would not transmit the lesions to the *Macacus rhesus* monkey, while saline extracts frequently did so. With first hand knowledge of how harmless urea is to normal tissues,³ I had no hesitancy in trying it on warts in human beings.

The results of urea treatment of warts have been good and warrant a more extensive trial of this therapeutic agent. A sterile 50 per cent solution of urea⁴ was used. From 0.1 to 0.3 cc was injected intracutaneously at the site of each growth, an attempt being made to get at the base of the wart but not far beneath it. In every one of the first 6 patients (nineteen warts) the growths were effectively and permanently removed, leaving practically no scar. From five to eighteen days was required for all evidence of the lesions to disappear. A number of colleagues then tried out the method, and results on a total of 16 patients were only about 50 per cent successful. Numerous growths required a second injection, and some appeared to be completely resistant. The exact site of injection may prove to be important. When the warts are numerous they appear to be more resistant than when only one or a few growths are present. No plantar warts were treated. I have recently treated 4 more patients, with good results except in 1, who had about twelve lesions on both hands. None of the warts were affected by the urea treatment.

I have noted elsewhere³ the occasional painful effect of strong solutions of urea in open wounds. The injection of the urea solution always led to some discomfort, but only rarely was the pain of any consequence. The pain was most severe in the treatment of warts at the nail edge, where the tissue is always

From the Scripps Metabolic Clinic

1 MacKay, E. M., and Schroeder, C. R. *Proc. Soc. Exper. Biol. & Med.* **35** 74, 1936

2 Wile, U. J., and Kingery, L. B. *The Etiology of Common Warts*, *J. A. M. A.* **73** 970 (Sept. 27) 1919

3 Holder, H. G., and MacKay, E. M. *The Use of Urea in the Treatment of Infected Wounds*, *J. A. M. A.* **108** 1167 (April 3) 1937, *Ann. Surg.* **110** 94, 1939

4 The Cutter Laboratories, Berkeley, Calif. prepared the urea solution and supplied it to me in small vials.

sensitive Menkin⁵ has found that concentrated urea may be an inflammatory irritant, which apparently accounts for the discomfort it sometimes produces. It is hard to believe that the irritation produced in human tissues is comparable to that observed by Menkin in the delicate tissues of the rabbit. Certainly the effect on the surfaces of wounds³ is not of this severe character.

After making my first trials I learned that Pietzsch⁶ had used a practically identical treatment for the removal of warts from horses. His results were excellent, and it is odd that the treatment has never been repeated in human beings before this. Pietzsch⁷ was prompted to try urea on warts in horses because of the hyperkeratosis in the lesions and the work of Stoeltzner⁸ and Stoye⁹. The latter observed that strong solutions of urea had a powerful softening effect on collagen and suggested the use of such solutions for softening or removing scar and binding tissues. The decided inflammatory irritating action of strong urea on rabbit tissues, as described by Menkin,⁵ must also be considered in connection with the method by which urea removes warts.

In attributing any specific mechanism to urea one must not forget that common warts differ tremendously in the difficulty of removal. Some disappear spontaneously or are removed by any of a variety of agents, and others resist almost all treatment. Whatever the mechanism involved in the removal of warts by urea, it is a therapeutic agent which appears to possess certain advantages over the usual escharotic agents and is worthy of an extended trial.

SUMMARY

A sterile solution of 50 per cent urea has been found useful for removing warts, when injected at their base in amounts of 0.1 to 0.2 cc. Some lesions resist this treatment, but most of them rapidly disappear. Urea therapy was tried because strong solutions of urea are virucidal, but it is uncertain that this virucidal action is the mechanism involved in the removal of warts.

476 Prospect Street

5 Menkin, V. *J. Exper. Med.* **56**:157, 1932.

6 Pietzsch, Z. *Ztschr. f. Veterinärk.* **39**:382, 1927.

7 J. L. Berliner, of the ammonia department of E. I. du Pont de Nemours & Company, brought the work of Pietzsch to my attention.

8 Stoeltzner, W. *München med. Wchnschr.* **72**:2133, 1925.

9 Stoye, W. *München med. Wchnschr.* **72**:2135, 1925.

Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

BLASTOMYCOSIS D B MARTIN and D T SMITH, *Am Rev Tuberc* 39.488, 1939

American blastomycosis is a distinct clinical entity, caused specifically by *Blastomyces dermatitidis*. Two types of infection caused by this fungus are recognized clinically: (a) cutaneous blastomycosis, a chronic or subacute ulcerating process, usually responding to treatment with iodides or radiation, and (b) systemic blastomycosis, a highly fatal disease, characterized by pulmonary infection and widespread distribution of lesions. The disease is more common in males. The serum of heavily infected patients discloses the presence of antibodies. In some patients a condition of hypersensitiveness to the fungus develops, which diminishes in the terminal stages of the disease. The degree of hypersensitiveness can be estimated by cutaneous tests and is materially reduced by repeated injections of minute doses of heat-killed vaccine. In some cases potassium iodide is curative, but it is a dangerous drug to administer to patients allergic to the fungus. In systemic blastomycosis iodide therapy should be started only after the state of hypersensitiveness has been excluded by cutaneous test or artificially reduced by therapeutic injections of vaccine.

ORAL TUBERCULOSIS J C BRYANT, *Am Rev Tuberc* 39 738, 1939

Tuberculous involvement of the oral cavity is comparatively rare, only 17 cases have been detected in some 7,000 cases of far advanced tuberculosis over a period of eighteen years. Tuberculous lesions of the tongue frequently follow mechanical irritation from the sharp edges of decayed and abraded teeth, broken fillings, gold inlays or crowns, or broken artificial teeth. The constant irritation and bathing of the oral tissues by the salivary and mucous secretions render the oral tissues highly resistant to tuberculous infection. Tuberculosis of the oral cavity is a secondary manifestation of a far advanced pulmonary condition with an unfavorable prognosis. When the prognosis is favorable, tuberculous lesions are seldom formed in tooth sockets after extractions, despite the presence of sputum heavily laden with the bacilli.

H J CORPER [ARCH PATH]

THE BACTERIOLOGY OF NORMAL SKIN. A NEW QUANTITATIVE TEST APPLIED TO A STUDY OF THE BACTERIAL FLORA AND THE DISINFECTANT ACTION OF MECHANICAL CLEANSING P B PRICE, *J Infect Dis* 63 301, 1938

Price utilized the method of washing the hands in a series of basins of water. By plating and culturing measured specimens of water, counting the colonies and multiplying by the total volume of water, the exact number of bacteria removed from the hands could be calculated. Scrubbings were done for the same length of time and in a uniform manner. Cumulative totals of organisms in the basins when plotted against time form a regular logarithmic curve which can be projected mathematically to zero. By studying data obtained in this manner the author came to the conclusion that cutaneous bacteria are of two sorts, "transients" and "residents." Transients, acquired mainly by contact, vary greatly in both number and kind. They may be abundant on exposed skin and under the nails but are relatively scarce on clean unexposed skin.

He stated the belief that resident bacteria form a comparatively stable flora. Forces increasing (chiefly by multiplication *in situ*) and decreasing their number tend to reach an equilibrium. Protected skin has as a rule a somewhat larger resident flora than exposed skin.

He found that after reduction (e g, by disinfection), reestablishment of the resident flora appears to proceed at a rate represented in general by a sigmoid curve, as is true of bacterial growths in cultures. Hands and arms thoroughly disinfected may require a week or more for complete reestablishment of the usual flora. Beneath clothing the general time is slightly shorter. Under sterile rubber gloves it is much shorter, the existing flora increasing rapidly, until it may exceed by far the ordinary flora.

Transient bacteria lie free on the surface or are loosely attached along with the dirt by fats, hence they are removed or killed with comparative ease. Resident organisms are more firmly attached and are far more resistant to attack by either detergents or germicides.

The transient flora may contain any number of pathogenic bacteria, the resident flora, relatively few as a rule. Certain contaminating organisms, however, seem able slowly to change status and become permanent residents of the skin. Consequently, prolonged or frequent exposure of the skin to contaminations may result in a resident flora containing many pathogenic germs. Such skin is not easily disinfected. Hands may thus become chronic carriers of virulent organisms.

Scrubbing with brush, soap and water removes the transient flora readily but the resident flora far more slowly. Scrubbing removes the bacteria from the hands and arms at a regular logarithmic rate that is constant, irrespective of the size of the original flora. The amount of bacteria is reduced, roughly, by one half each six minutes of scrubbing. The largest variable affecting this rate is the amount of vigor used in brushing, the sort of soap used and the sterility and temperature of the water washed in are less important factors.

COMPARISON OF INFECTION OF MICE BY MYCELIAL AND YEAST FORMS OF *BLASTOMYCES DERMATITIDIS* R D BAKER, *J Infect Dis* 63:324, 1939

The author was interested to learn whether equivalent doses of the mycelial form of *Blastomyces dermatitidis* were as infectious as the yeast form. He injected both forms of the organism into mice. In his experiments the mycelial form of a strain of *B dermatitidis* was found to be as effective as the yeast form in causing death of mice and in producing extensive lesions in the abdominal cavity and lungs when weighed equivalent doses were given intraperitoneally. The aerial growth of the mycelial form was as effective as the subsurface growth of the mycelium. When examined at the spontaneous death of the animals the lesions always contained the yeast form even when the mycelial form had been injected.

CORNBLEET, Chicago

OBSERVATIONS ON SENSITIVITY TO POISON IVY FRANK A SIMON and EDWARD LOTSPEICH, *J Invest Dermat* 2 143 (June) 1939

Again it is shown that application to the skin of weak dilutions of extract of poison ivy does not produce a reaction in all persons. Some of the persons who reacted to the cutaneous tests for poison ivy were then given a series of intramuscular injections of the concentrated ivy extract. After this the cutaneous tests were repeated, but no change in the reaction was observed. Calamine lotion, 5 per cent potassium permanganate and 5 per cent lead acetate were used to treat some of the patients with induced poison ivy dermatitis. The evolution of the lesions was seemingly unaltered by any of these topical applications.

DAVIS, Nashville, Tenn

SIGNIFICANCE OF SEX HORMONES IN TANNING OF THE SKIN OF WOMEN J B HAMILTON, *Proc Soc Exper Biol & Med* 40 502 (March) 1939

Five women, of whom 2 were at the menopause, 2 had undergone bilateral ovariectomy and 1 had undergone hysterectomy, were given either estrone (theelin) or testosterone propionate for various intervals. Study of the color of the skin

revealed that all 5 women exhibited increased coloration of the skin within a few days after receiving the estrogen or the androgen

HANSEN, Minneapolis [AM J DIS CHILD]

RETROBULAR NEURITIS WITH PELLAGRA IN NIGERIA D F MOORE, J Trop Med 42 109 (April 15) 1939

Moore discusses a syndrome that occurs extensively in southern Nigeria. It consists of perleche, soreness of the tongue and genitalia and retrobulbar neuritis associated with optic atrophy. The condition has responded dramatically to treatment with autoclaved yeast products and so is believed to be pellagrous. It is believed that gari, a dried, parched manioc food, plays an important part in its incidence. The facts in support of pellagra as the cause of the syndrome in southern Nigeria are that (1) throughout the palm oil belt there is an abundance of cheap edible oil, (2) no single case of xerophthalmia has been seen in southern Nigeria, (3) there is a great relative shortage of animal and fish protein in southern Nigeria (it is in these areas, or under conditions that permit this shortage, that this syndrome is found) and (4) when gari is eaten to excess in the absence of the protein protective foods it is shown to have an almost constant relation to the incidence of this syndrome. Gari bears a strong suggestive resemblance to "spoiled maize." A nutritional policy for Nigeria based on the recommendations of the League of Nations Health Committee (1937) is required to include particularly the development of local food sources and when possible to abolish by replacement both gari and stockfish as dietary essentials of the people.

J A M A

THE ROLE OF THE SYMPATHETIC NERVOUS SYSTEM IN REACTIONS TO ARSENICAL CHEMOTHERAPY A TZANCK and LEWI, Bull Soc franç de dermat et syph 46 751 (May) 1939

The authors devote approximately 50 pages to a detailed consideration of the subject. They emphasize the fact that the study of the sympathetic nervous system in relation to arsenical therapy is extremely difficult. The functional exploration of the sympathetic nervous system is delicate, and the results obtained by methods of study are not beyond criticism. This is especially true in studies of arsenical reactions, since these reactions are so variable.

The authors mention briefly tests of the various reflexes and pharmacodynamic tests employing epinephrine, atropine and pilocarpine, stating that unfortunately such tests do not determine the condition of the terminal nerves and that the results with regard to the higher centers are sometimes paradoxical or contradictory. On the other hand, such tests carefully performed and frequently repeated have given information of real value in anaphylactic shock and infectious diseases.

Tzanck and Lewi believe that the vegetative nervous system is related to arsenical reactions in three ways:

1. In certain cases it can exert an influence during the course of sensitization of an organism to the drug. The autonomic system in these cases seems to intervene in a latent way during the period of incubation which separates the beginning of the sensitization and the appearance of the reactions.

2. In other cases, the clinical aspect or evolution of the reactions suggests a direct shock to the sympathetic nervous system. These cases are characterized by the rapid appearance of the condition and the response in some instances to drugs which influence the nervous system (nitritoid crisis).

3. Finally, in certain cases the intervention of the sympathetic nervous system is manifested at the same time as the reaction itself, rather than during the incubation period. Erythema of the ninth day is cited as an example of this type of reaction.

The authors draw the following conclusions

1. Purely toxic reactions following arsenical chemotherapy are not influenced in their genesis by the sympathetic nervous system. These accidents occur after too large doses of the drug have been received

2 "Infectious" reactions (biotropism) may be influenced to a certain extent by the sympathetic nervous system

3 Most reactions following arsenotherapy seem to be due to individual intolerance. It is this group which is most strongly influenced by the sympathetic nervous system

The nitritoid crisis and the more common arsenical shock are thought to be related to a certain extent to the sympathetic nervous system. Authentic nitritoid crises could not be produced in experimental animals

Tzanck and Lewi believe that the rapid onset and sudden involution of the slightly delayed reactions, such as fever of the ninth day, various fleeting eruptions and meningeal reactions, suggest a disturbance of the nervous regulation as well as actual disturbance of the parenchyma of the various organs affected

The authors are of the opinion that in the late arsenical reactions, such as erythroderma, the role of the vegetative nervous system is secondary to actual hypersensitiveness of the tissues, although the sympathetic nervous system probably exercises some influence on the genesis of this hypersensitiveness

In general, just as the reactions following chemotherapy vary among themselves so vary the types of influence exercised by the sympathetic nervous system (functional role, dystrophic role and reactional role) LAYMON, Minneapolis

DERMATOSTOMATITIS H HULLSTRUNG, *Dermat Wchnschr* **107.1041** (Aug 27) 1938

Hullstrung describes a man aged 51 who had ulcerative stomatitis and superficial ulcers on the inner surface of one thigh and on the scrotum. Several bullae were noted in the left inguinal fold. The condition cleared in about four weeks with symptomatic treatment. In less than two months it recurred, more severe than the first attack, and cleared in about six weeks. The author concludes that the condition is a disease sui generis rather than a variety of erythema multiforme, chiefly on account of the localization and the fact that it occurred in a patient past middle age

HISTAMINE-LIKE EFFECT OF IRRADIATED OR INFLAMMATORY SKIN FRIEDRICH VOSS, *Dermat Wchnschr* **107:1115** (Sept 17) 1938

The author observed that roentgen ray irradiation of the rat caused an increase in the gastric acidity and if continued a decrease to anacidity. Repeated injections of histamine produced the same effect. Voss had previously found normal gastric acidity in cases of localized dermatoses, while in the early stages of extensive eruptions hyperacidity was the rule, which changed to hypoacidity if the eruption became chronic. He concludes that irradiation or other means of causing inflammatory reactions in the skin produce histamine, and the changes in the gastric secretion are a histamine effect

THE DIAGNOSIS OF SYPHILIS FROM A SINGLE DROP OF BLOOD BY THE CHEDIK-DAHR METHOD MARIA GRAHNER and MARGARETE BERTRAM, *Dermat Wchnschr* **107 1119** (Sept 17) 1938

The authors describe the Dahr modification of the Chediak test, which they used in testing 400 serums. With blood of patients with primary and latent syphilis the test was more sensitive than the other standard tests, while in patients in other stages of the disease the results were comparable. One false positive reaction occurred, and 3 reactions were doubtful

AUTOHEMOTHERAPY FOR ACANTHOSIS RUBRA LICHENOIDES ANTONIO RISI, Dermat Wchnschr **107** 1142 (Sept 24) 1938

The author describes the case of a woman aged 28 in whom had developed a symmetric eruption involving the axillas, vulva and nipples fifteen years previously. The eruption was made up of crythematos small lichenoid papules and was severely pruritic. Microscopic examination of tissue showed hyperplasia of the epidermis, polymorphonuclear leukocyte infiltrate and dilatation of the sweat glands. The eruption and pruritus were resistant to all forms of treatment previously tried. Risi named the condition acanthosis rubra lichenoides. It responded to a series of thirty intramuscular injections of the patient's own blood. (Photographs, clinical description and pathologic description suggest Fox-Fordyce disease—Abstracter.)

AUTOHEMOTHERAPY FOR ACANTHOSIS RUBRA LICHENOIDES DIAGNOSTIC COMMENTS ON THE ARTICLE BY ANTONIO RISI (Dermat Wchnschr **107** 1142 [Aug 27] 1938) SEPP TAPPEINER, Dermat Wchnschr **107** 1487 (Dec 17) 1938

Tappeiner briefly reviews Risi's article and concludes that the condition described was an example of Fox-Fordyce disease.

PATHOLOGY OF UNILATERAL HYPERHIDROSIS OF THE FACE OF CENTRAL ORIGIN LADISLAUS VAMOS, Dermat Wchnschr **107** 1147 (Sept 24) 1938

Vamos studied a man aged 36 who presented severe hyperhidrosis of the left side of his face and neck. He had had influenza nineteen years before, followed by encephalitis, during the course of which he had difficulty resisting sleep. After that he noticed that the left half of his face perspired unusually when exposed to heat. Ten years later, after a mental upset due to household difficulties, the severity of the condition increased. The disease is ascribed to a partial lesion of the parasympathetic center due to damage of the thalamus from the encephalitis.

EXPERIMENTAL RESEARCH INTO THE CURATIVE EFFECT OF PHYSICALLY INDUCED HYPERTHERMY A BESSEMANS, Dermat Wchnschr **107** 1161 (Oct 1) 1938

The author reports the effect of various methods of local and generalized application of heat in the treatment of syphilis in laboratory animals and in human beings. He concludes that the important factors are sufficient heat and its application for sufficient time. The first effect of the increased temperature is a decrease in virulence of the organisms, followed by a decrease in motility and finally by their disappearance.

TREATMENT OF PEMPHIGUS WITH LIVER PREPARATIONS ROLF KYSER, Dermat Wchnschr **107** 1170 (Oct 1) 1938

Kyser reports briefly on 4 patients with pemphigus who were treated with liver extract. One died of circulatory failure at the age of 88. The other 3 have been without recurrence of the disease for from six to twenty-four months. Four cases in which treatment was successful were found in the literature.

MEASURABLE PHYSICO-CHEMICAL CHANGES IN HAIR AS THE RESULT OF THERAPEUTIC AND COSMETIC APPLICATIONS ALFRED MARCHIONINI and LIESELOTTE DRAESEKE, Dermat Wchnschr **107** 1201 (Oct 8) 1938

By means of the apparatus devised by Marchionini and Aretz the extensibility and fragility of hair exposed to various therapeutic and cosmetic substances were tested. It was found that acid applications, such as salicylic acid preparations and henna solutions, had but little effect, while alkaline substances, such as therapeutic soap shampoos, bleaches and permanent waving, altered the keratin substance to decrease the elasticity of the hair and increase the tendency to break.

TEMPERATURE MEASUREMENTS IN THE NEIGHBORHOOD OF ACROCYANOSIS AND LUPUS VULGARIS HELLMUT HECHT, *Dermat Wchnschr* 107:1221 (Oct. 15) 1938

The author describes a sensitive thermoelement, by which it is possible to measure the temperature of a small area of skin. In 4 patients with acrocyanosis the temperature of the skin of the hands and nearby areas was low, approaching that of the air (20 to 21 C). After immersion of the hands in cold water (18 C) for five minutes there was a decrease in temperature lasting twenty minutes, indicating arterial spasm. Measurements in the immediate neighborhood of lesions of lupus vulgaris showed lower figures than those of the other portions of the skin.

XANTHOMA MOLLUSCIFORME ET GENERALISATUM IN AN INFANT DESIDER STEIGER-KAZAL, *Dermat Wchnschr* 107 1230 (Oct 15) 1938

An infant 19 months old presented a generalized nodular eruption, in which the lesions were pink, and an umbilication suggestive of molluscum contagiosum. The lesions had been present at least three months, and the history suggested that a few had been present since birth. The scalp and buccal mucosa were involved. Microscopic examination showed the pathologic picture of xanthoma. The sugar content of the blood was normal, and the cholesterol content was somewhat low.

THE FIRST CASE OF ANGIOKERATOMA CORPORIS DIFFUSUM IN JAPAN YOSHIO TAGUCHI, *Dermat Wchnschr* 107 1281 (Oct 29) 1938

Taguchi's patient was a 27 year old man who had first noticed the development of red spots around his knees eleven years before. New lesions had developed gradually until they were sparsely scattered on the legs, thighs, arms, forearms and trunk. The lesions were warty, dark brown to black and the size of a split pea. Microscopic examination of sections showed dilated blood vessels and capillaries, with lacunas and cavernous areas filled with thrombi extending into the epidermis. There was also hyperplasia of the sweat glands in the vicinity of the lesion.

A CASE OF ERYTHEMA EKSUDATIVUM MULTIFORME GIGANTEUM PAUL JOBST, *Dermat Wchnschr* 107:1284 (Oct 29) 1938

Jobst reports on a patient who had typical erythema multiforme of the hands and forearms. She presented an immense lesion on each leg, resembling Darier's erythema annulare centrifugum. The course of the disease was that of erythema multiforme.

AMBULATORY SUBOCCIPITAL (CISTERNAL) PUNCTURE MICHAEL KRAUS, *Dermat Wchnschr* 107.1305 (Nov 5) 1938

The author has performed more than a thousand cisternal punctures. He considers this procedure preferable to lumbar puncture. Obesity, hypertension and old age increase the difficulty of the procedure somewhat but are not contraindications. A few nervous anemic patients with increased vasolability fainted, but they might also have fainted if intramuscular or intravenous puncture had been used. The author prefers the patient in a sitting position for cisternal puncture.

HERPES ZOSTER ANALIS ANTONIO SPRECHER JR, *Deimat Wchnschr* 107.1376 (Nov 19) 1938

The author describes a case in which herpes zoster developed in the region of the anus and extended onto the left thigh. The third, fourth and fifth sacral nerve roots were involved.

TAUSSIG, San Francisco

Society Transactions

MINNESOTA DERMATOLOGICAL SOCIETY

E M RUSTEN, M D, *President*

F W LYNCH, M D, *Secretary*

Rochester, Sept 24, 1939

Presentation of all cases at this meeting was made by Dr Paul A O'Leary, Dr Hamilton Montgomery and Dr Louis A Brunsting, of Rochester

Rosacea-Like Tuberculid of Lewandowsky

A married woman aged 34 came to the clinic because of dermatosis of the cheeks, which had been present for two and a half years. She also had chronic nervous exhaustion. Roentgenologic examination of the thorax and gallbladder and analysis of the gastric contents did not disclose any abnormality. The patient said that a sister had pulmonary tuberculosis. Treatment for acne rosacea did not produce any response. The histologic examination of a specimen obtained from the preauricular region was suggestive of rosacea-like tuberculid of Lewandowsky. Twenty injections of gold sodium thiosulfate also failed to produce any improvement. The result of a tuberculin test with purified protein derivative was negative with the weak concentration and positive with the strong.

DISCUSSION

DR H E MICHELSON, Minneapolis. I have been much interested for some time in patients with lesions of the face the microscopic picture of which made possible a diagnosis of some form of tuberculosis. I am not sure whether the term "rosacea-like tuberculid" should be used, because it implies that the lesions must definitely resemble rosacea and must run the clinical course of a tuberculid. In most of the cases in which I have made such a diagnosis the course much more resembled that of lupus miliaris disseminatus faciei. I do not believe that the tuberculin test is a criterion for diagnosis here, and I want to stress that the time for cure or resolution is long. In the patients that I have observed one or two years must be anticipated. I have had some good results with injections of a gold compound and some disappointments.

Lupus Vulgaris

A man aged 78 has had an eruption on his left arm for seventy-four years. In this period the lesion has changed only slightly. The patient had diphtheria thirty years before he came to the clinic. Prostatectomy has been performed. He has hypertension of moderate degree. There is no evidence of tuberculosis elsewhere in the body. On the left arm is a large plaque with peripheral nodules. Diascopic examination disclosed an apple jelly hue of the nodules. There is evidence of definite activity at the inferior border of the lesion, where numerous satellite apple jelly nodules are present. More centrally atrophy, telangiectasia and dry scaling are seen. Examination of a specimen of the lesion revealed typical lupus vulgaris.

DISCUSSION

DR PAUL A O'LEARY, Rochester. The main reason for presenting this case is that the eruption has been present for seventy-four years.

DR H E MICHELSON, Minneapolis I should like to ask if any one has had any success in the excising and grafting of lupus vulgaris

DR PAUL A O'LEARY, Rochester Our experience in the excising and grafting of lupus vulgaris has been unsatisfactory A young woman had a small plaque (5 cm in diameter) of lupus vulgaris of four months' duration, which seemed an ideal type for surgical treatment The area was widely excised, and a full thickness skin graft was immediately applied The graft was successful, but four months later the lupus nodules recurred in the scar surrounding the graft and shortly thereafter they invaded not only the graft but the surrounding skin Excision and grafting in 2 other patients with lupus vulgaris were equally unsuccessful

Group of Cases of Lupus Erythematosus

CASE 1—*Subacute Disseminate Lupus Erythematosus*

A woman aged 46 came to the clinic on Sept 18, 1939, because of dermatitis of the face and arthritis In 1927 the value for the hemoglobin was 56 per cent, liver was administered at this time In 1933 stiffness and pain on motion developed in her right shoulder Her hands became stiff, and generalized arthralgia developed In August 1933 facial "eczema" developed, this lasted throughout the following winter She had a transitory eruption on her face in 1934, lasting a few months In 1936 she had arthritis, which was associated with a temperature of 104 F Twelve injections of typhoid vaccine were administered at this time, vaccine therapy and massage also have been employed In March 1939, after frostbite, a generalized eruption appeared on her face, which has increased in severity and has been aggravated by exposure to sunlight

The patient's teeth and tonsils have been removed Examination did not reveal any evidence of true intra-articular disease Periarticular thickening was present in the proximal and midphalangeal joints, but this was minimal in amount and did not interfere with motion Examination discloses tender regions on the elbows and knees and swellings of the synovial membrane Both shoulders are slightly painful on motion, and there is slight interference with dorsiflexion of the wrists Examination of the skin shows changes of the erythema faciei perstans type of lupus erythematosus The patient has no fever The concentration of hemoglobin was 12.9 Gm per hundred cubic centimeters of blood The erythrocyte count was 4,100,000 per cubic millimeter, and the leukocyte count, 5,800 A differential leukocyte count revealed 26 per cent lymphocytes, 10 per cent monocytes, 58 per cent neutrophils and 6 per cent eosinophils The coagulation time of the blood was six minutes. Roentgenologic examination of the thorax disclosed pleuritic adhesions at the left costophrenic angle Roentgenograms of the wrists, hands, shoulders, elbows and knees do not show any abnormality The urine was normal Examination of a specimen of the facial lesion revealed the typical picture of subacute disseminate lupus erythematosus

CASE 2—*Subacute Disseminate Lupus Erythematosus*

A married woman aged 32 came to the clinic in May 1939 In the summer of 1938, after a sunburn, the patient noticed a spotted eruption on her face The condition was diagnosed as lupus erythematosus Treatment included a variety of supportive measures, injections of a bismuth compound and of a gold sodium thio-sulfate, fifteen fever treatments with the hypertherm and administration of sulfanilamide The sulfanilamide produced toxic jaundice

Examination at the clinic revealed discrete inflamed plaques, 0.5 to 1 cm in diameter, about the mouth, over the upper part of the chest and back and on the left hand and forearm An extensive sunburn, associated with vesiculation, was present on the right forearm, which had been exposed to the sun for fifteen or twenty minutes on the day before the patient came to the clinic Urinalysis disclosed mild albuminuria The leukocyte count varied from 4,200 to 7,000 per cubic millimeter of blood A differential leukocyte count revealed 35 per cent lymphocytes, 4 per cent monocytes and 61 per cent neutrophils Roentgenographic examination of the teeth showed periapical infection at two sites Rest in bed and

avoidance of exposure to light for three months improved the condition of the skin materially. A perirectal abscess which developed in July was treated surgically. Two infected teeth were removed on separate occasions, without reaction. Reexamination of the blood from time to time has revealed persistence of the relative lymphocytosis. The patient has had occasional attacks of mild arthralgia in the left shoulder. For several weeks before presentation of the case small doses of gold sodium thiosulfate have been administered intravenously and have been well tolerated.

CASE 3—*Acute Disseminate Lupus Erythematosus*

A woman aged 27 has an eruption on the eyelids and on the upper part of the back and chest, which developed after exposure to sunlight two months before she came to the clinic. For two years previously she suffered intermittently from polyarthritis and Raynaud's disease. In the treatment of the arthritis, the tonsils and two infected teeth were removed, sulfanilamide was administered but has not been well tolerated.

When the patient was first seen at the clinic she had a fever and was suffering from general malaise and polyarthritis. Examination revealed a light red papular eruption on the eyelids and an extensive eruption on the upper part of the back and chest. Urinalysis disclosed persistent albuminuria, hematuria and hyaline and granular casts, the specific gravity of the urine varied from 1.010 to 1.011. The concentration of urea varied from 34 to 64 mg per hundred cubic centimeters of blood. The urea clearance was normal. The concentration of total protein was 5.2 Gm per hundred cubic centimeters of serum, and the albumin-globulin ratio was 1:1.5. The concentration of serum sulfate was 97 mg per hundred cubic centimeters, and the value for the creatine was 16 mg per hundred cubic centimeters of blood. The sedimentation rate of the erythrocytes was 130 mm in one hour. The concentration of hemoglobin was 10.2 Gm per hundred cubic centimeters of blood. The leukocyte count ranged from 3,800 to 7,200 per cubic millimeter. A differential blood count did not reveal any abnormality. The fever has persisted, and the temperature recently has increased in degree. The diagnosis in this case is acute disseminate lupus erythematosus associated with anemia, polyarthritis and severe nephrosis.

CASE 4—*Lupus Erythematosus of Scalp, Secondary Folliculitis*

A white man aged 52 came to the clinic because of an eruption on the scalp which has been present for approximately nineteen months. He had consulted a Canadian dermatologist, who had made a diagnosis of lupus erythematosus. Moderate improvement followed the administration of a few injections of gold sodium thiosulfate, but a pustular perifolliculitis developed at the involved site a few months after this treatment was discontinued. The past history disclosed that the patient has had "bronchial trouble," allergic rhinitis and migraine. The lesions are of two types: (1) a rather superficial pustular perifolliculitis, which consists of not more than a dozen individual lesions situated near the occiput of the scalp, and (2) deeply infiltrated and atrophic plaques, which are limited to the "hatband" region laterally and posteriorly and are associated with follicular plugging, patulous follicles, scaling and telangiectasia. Complete alopecia and atrophy of the skin are the only changes noted in some regions. Roentgenologic examination of the thorax did not disclose any abnormality.

DISCUSSION

DR PAUL A. O'LEARY, Rochester. This group of patients with various manifestations of lupus erythematosus is presented to reemphasize the fact that the morphologic features of the disease are multiform and that the systemic features may vary from a banal asymptomatic scalp lesion to a severe generalized disease that frequently results in death. In this group of cases we have endeavored to bring out the point that arthralgia, often of a severe degree, is frequently observed in patients with this disease, in fact, in our experience, in the disseminate form the onset is often with pains and swellings in the joints but with no appreciable

roentgenographic evidence of osseous changes. The presence of leukopenia in association with arthralgia and a mild fever should arouse one's suspicion of the possibility of beginning disseminate lupus erythematosus.

There was evidence of chronic dissemination in the second patient of this group in addition to the severe sunburn. She had been given fifteen hypertherm treatments in addition to sulfanilamide before coming under our care. After this treatment the patient remained in bed in a dark room for three months, and when she returned to the clinic the lesions had become localized, as in discoid lupus erythematosus. It is difficult to appraise the value of the fever therapy or the other measures for this patient. She is now undergoing a course of treatments with a gold compound and is showing improvement.

In contrast, I recently saw a girl in whom disseminated lupus erythematosus had started two months previously as severe generalized arthralgia with leukopenia (2,000 white blood cells per cubic millimeter). She received one hypertherm fever treatment, which was immediately followed by the appearance of an extensive eruption of disseminate lupus erythematosus and all its systemic complications, from which she died some two weeks later.

In other words, fever therapy for disseminate lupus erythematosus is an extremely hazardous procedure, the results of which do not justify the risk. I question the relation between the chronic discoid type and the acute disseminate type of the disease. The former, with a long life expectancy and few systemic complications, and the latter, with the short life expectancy and autopsy evidence of extensive toxic changes in the viscera, have little in common.

DR HENRY E. MICHELSON, Minneapolis. I think that most of those who have been dermatologists for some time are impressed with the change of viewpoint with which isolated lesions in lupus erythematosus are looked on, and I believe that this is entirely due to the fact that a new therapy has been acquired. As long as the lesions were treated entirely locally the condition was considered a local disease. But now I am sure that lupus erythematosus is looked on as a systemic disease in which there is a great variation of signs and symptoms. In a general way it can be likened to sarcoid, because of the chronicity of the various findings, the resistance to most of the remedies and the relapses. With acute lupus erythematosus the comparison to sarcoid is not so striking, but the systemic character is again emphasized.

DR S. E. SWEITZER, Minneapolis. This group of cases shown today emphasizes the fact that many years ago, when I first took up dermatology, acute lupus erythematosus was almost never seen, most examples were of the chronic discoid type, and one did not have much fear of the condition. From these cases a variety of differences can be seen in the same disease. A beginner would swear that they did not have any connection at all. The more cases of lupus erythematosus are observed, the more dangerous the disease seems. It is poorly treated by the average general practitioner and sometimes by the dermatologist, they do not have any respect for the difficulties they may get into. After three or four months in the dark and after the teeth were pulled, the second patient of this group showed a discoid lupus erythematosus. Foci have a great deal to do with the process. Often removal of abscessed teeth will cause an improvement. It seems to me that the younger physicians when a patient with lupus erythematosus comes into the office should think of what this disease is and should certainly advise the patient to stay away from sunlight because of the danger of overexposure. The more I see of lupus erythematosus the more I fear it.

DR STEPHAN EPSTEIN, Marshfield, Wis. (associate member). A statistical survey of the cases of lupus erythematosus from 1925 to 1934 at the University Skin Clinic in Breslau showed that the incidence of pulmonary tuberculosis in patients with lupus erythematosus was far below that found in patients with tuberculosis and tuberculids of the skin. The figures were somewhat higher but not very different from those of the controls.

I have the impression that American dermatologists are inclined to believe that the tuberculous origin is generally accepted in the Continental European countries. This holds true for the French and part of the Swiss and Viennese schools, the majority of German dermatologists, however, do not favor this hypothesis.

DR HAMILTON MONTGOMERY, Rochester In the first case there were definite signs of arthralgia for six years before the development of lupus erythematosus, although the patient said she had had transitory erythema of the face on two occasions.

In a recent study of 154 patients with disseminate types of lupus erythematosus seen at the clinic, I found that 5 per cent of those with the chronic disseminate type (generalized discoid), 27 per cent of those with the subacute disseminate type and 33 per cent of those with acute disseminate lupus erythematosus had prodromal symptoms, especially malaise, arthralgias and transitory fever. Considering arthralgia or arthritis by itself in association with lupus erythematosus or preceding it, 20 per cent of those with the chronic disseminate type, 50 per cent of those with the subacute disseminate type and 33 per cent of those with the acute disseminate type had arthritis or arthralgia. A similar increase in frequency occurs in cases of lupus erythematosus, in regard to other systemic symptoms, the more acute the process is. The extent of cutaneous involvement does not parallel the severity of the disease or the degree of systemic involvement.

In regard to mortality, 8 per cent of the patients with the chronic disseminate type and 47 per cent of those with the subacute disseminate type have already died of the disease. Only 2 of the 30 patients with acute disseminate lupus erythematosus are still alive. In each of these the disease is of less than a year's duration.

DR LOUIS A. BRUNSTING, Rochester No adequate explanation has been made for the phenomenon of sensitivity to light in patients with disseminated lupus erythematosus. The porphyrin metabolism is not abnormal except when fever is present.

The most significant item in prognosis is the level of the leukocytes, leukopenia being a constant observation. Nephritis is a serious complication in the terminal stage, nevertheless, on postmortem examination there is rarely gross pathologic change in the kidneys.

DR PAUL A. O'LEARY, Rochester Dr Sweitzer's remarks about the seriousness of lupus erythematosus are sympathetically shared. Tuberculosis has become increasingly less significant as an etiologic agent as other bacterial infections and photosensitivity have become more prominent.

Tinea Capitis Kerion Celsi

A boy aged 13 came to the clinic because of kerion Celsi. The lesions, which first appeared in July 1939, involve the scalp, forehead and cheeks. The lesions of the skin are associated with edema of the eyelids, enlargement of the cervical lymph nodes, fever and a systemic reaction. The application of wet antiseptic dressings and ointments did not produce a satisfactory response. Roentgen therapy was employed the last of July and the middle of August, and this produced satisfactory involution of the lesions.

Tinea Capitis Kerion Celsi Trichophytid

The patient, a girl aged 10 years, is a sister of the preceding patient. She had typical kerion Celsi which was limited to the scalp. The lesion first appeared about Sept 1, 1939. It was associated with fever and enlargement of the regional lymph nodes. Treatment has consisted of the use of antiseptic dressings and one thorough application of solid carbon dioxide to the affected region. A week ago extensive follicular trichophytid developed on the shoulders, arms and upper part of the trunk.

DISCUSSION

DR WALTER POPP, Rochester The boy was first seen on July 31 and was given roentgen ray treatments to each area of involvement, with 2 mm of aluminum filtration and voltages generated at 100 kilovolts The output for each field was approximately 225 r in air The treatment was repeated two weeks later, using the same technical factors This amount of irradiation is not sufficient to produce the epilation seen in this patient The epilation is probably due to the combination of roentgen rays and local applications There is no reason to assume that the epilation will be permanent in this patient, as there is definite evidence of regrowth of hair

DR HENRY E. MICHELSON, Minneapolis I have observed that in patients in whom the inoculation was from animals the response to treatment is good I see such patients most of the time and rarely ever use roentgen rays Strong keratolytic ointments, freezing with solid carbon dioxide and sometimes compresses are all that I have found necessary

DR CARL LAYMON, Minneapolis The favorable results mentioned by Dr. Michelson which are obtained in this vicinity are undoubtedly due to the fact that in the great majority of cases of ringworm of the scalp the condition is fortunately caused by fungi of animal origin George Lewis and others have emphasized frequently that conditions of this type rarely require epilation by roentgen rays and eventually heal as a result of local therapy

Localized and Linear Scleroderma, Atrophic and Indurated

A Jewess aged 23 came to the clinic in September 1939 because of stiffness of the hands and feet, thickening of the skin of the extremities and pain in the hands, shoulders and knees The general health of the patient has been excellent, but she has complained of cold hands and cold feet for several years In February 1938 a diffuse macular rash first developed above the right lower extremity, and about the same time raised thickened portions of skin appeared in the right palm In May she first consulted her physician in her home locality, at which time there were groups of lichenoid lesions in zosteriform arrangement extending from the right breast and the right scapular region down the right arm and forearm and onto the palm and the fourth and fifth fingers of the right hand The anterior surface of the calf of the right leg was also involved These lesions resembled those of zosteriform lichen planus to such an extent that a diagnosis of this disease was made, and treatment was begun accordingly The patient was dismissed on July 12 She reappeared on August 30 because of a recurrence of lichen planus on the fourth and fifth fingers of the right hand At this time she had a noninflammatory but painful swelling on the right forearm and on the back of the right hand There was a discrete lymph node in the right axilla By September 1 all the former lichen-planus-like lesions had come to resemble guttate scleroderma and for the most part have continued that way since By November there was an extension of the lesions to the left side of the body, and those on the right side became confluent A generalized acute scleroderma then developed, this involved chiefly the upper and lower extremities This has subsequently subsided and formed the present clinical picture Examination elsewhere of a piece of muscle which was removed for biopsy showed normal muscle with the exception of calcium deposits, and examination of a section of skin revealed acute scleroderma

Her condition remained about the same until January 1939, at which time white atrophic spots developed on the breasts, neck and shoulders In the past six to eight months there has been a tightening of the skin of the legs up to the knees In the past six weeks the left arm has become involved The patient has some difficulty in walking and feels tired all the time She has not lost weight and has had no fever or other systemic symptoms The result of neurologic examination was essentially negative Erythrocytes numbered 4,230,000 per cubic millimeter

of blood, and leukocytes, 1,900 per cubic millimeter. The basal metabolic rate was —9 per cent. The concentration of creatinine was 12 mg per hundred cubic centimeters of blood. Roentgenologic examination of the thorax revealed a Ghon complex on both sides. The value for the calcium was 9.9 mg per hundred cubic centimeters of serum. The sedimentation rate was 30 mm in one hour.

DISCUSSION

DR PAUL A. O'LEARY, Rochester. I believe that it is agreed that this patient has several manifestations of scleroderma, including the atrophic plaques. It is of interest that a competent dermatologist made the diagnosis of lichen planus several months before the appearance of the scleroderma.

Acrodermatitis Chronica Atrophicans.

A laborer aged 69, who was born in Sweden, came to the clinic because of pruritus. He had had an eruption on his legs for approximately twenty years. The pruritus was particularly severe on the legs, but at times it has been generalized. The history was difficult to elicit and evaluate. Examination reveals a symmetric dermatosis involving the posterior part of the thighs and the buttocks but sparing the perianal region. It extends posteriorly and laterally over the thighs and encircles the legs completely in the neighborhood of the knees. Examination reveals a dusky erythematous marking on the dorsa of the feet. A fine superficial wrinkling of the skin is present on the affected regions of the thighs and buttocks. The lesions are prominent about the knees, where the skin is loose and wrinkled and has the appearance of the skin of a baked apple; the underlying subcutaneous tissue is soft and loosely adherent. A small pale doughy nodule, about 4 by 8 mm, is present on the medial aspect of the right knee. There is no evidence of atrophy in the lower portion of the leg, where the skin is thick and slightly adherent, nor is there evidence of sclerosis. Excoriations are present. Examination of the blood disclosed a moderate grade of hypochromic anemia. The concentration of hemoglobin was 10.3 Gm per hundred cubic centimeters of blood. The erythrocyte count was 3,500,000 per cubic millimeter of blood. Other laboratory tests did not reveal any abnormality. A specimen which was removed for biopsy was unsatisfactory.

DISCUSSION

DR R. R. SULLIVAN, Minneapolis. This case presents a typical clinical picture of *acrodermatitis chronica atrophicans* in its terminal or atrophic stage. The characteristic distribution, the parchment-like, easily wrinkled skin and the prominence of the underlying blood vessels secondary to the atrophy are all well demonstrated here. There are no inflammatory infiltrations, bandlike formations or tumors to be seen. Of interest, however, is the sclerotic, hard, scleroderma-like state of the skin on the lower third of each leg, the ankle and the dorsal surface of the foot. Though sometimes confused with it, this process in cases of *acrodermatitis chronica atrophicans* is believed to be quite distinct from true scleroderma. As one might suspect, patients with this condition not infrequently are subjected to injections for what appear to be varicose veins, usually without benefit.

Although this patient was born in Europe, I believe too much emphasis has been placed on the place of birth. Cases reported in the American literature have represented so many different countries of Europe that any significant relation to place of birth does not appear reasonable. Moreover, the disease has been reported in a substantial number of persons born in this country, although the majority of cases reported in American literature have admittedly been in European-born persons. Recent reviews of the literature, including the foreign, have not been productive of any new contributions to either the causation or the problem of treatment.

A Case for Diagnosis (Angioma Serpiginosum?).

A single man aged 24 came to the clinic Sept 21, 1939, complaining of a generalized erythematous speckled rash, which had been present for ten or twelve years. The patient recalled that he had had pinpoint red dots over the chest and outer part of the arms at the age of 12 years. He stated that his body might have been flushed at that time, but he was not certain. Five or six years ago the flushing of the body became more prominent, as did the speckling of the skin. In warm weather the lesions are less prominent, and in cold weather, more prominent. Cold water accentuates the lesions. There has been a day to day variation, depending on the temperature of his environment. Likewise, the lesions are more prominent after exercise. The sun has no effect on the lesions, the skin apparently tanning normally. In the past several years the flushing of the skin has become more prominent, especially about the upper part of the trunk, the arms, the inner part of the thighs and the back. He states that he has not taken any drugs with the exception of acetylsalicylic acid and that he has no occupational contact with drugs or chemicals. His general health has been excellent, however, he states that he has been short winded for several years but that there has been no actual dyspnea. The family history is essentially not significant; the parents, brothers or sisters have never had a similar cutaneous disease. There is no hypertension or other circulatory disease.

The results of general examination were essentially negative with the exception that the blood pressure was 144 mm of mercury systolic and 94 mm diastolic and that there was a questionable enlargement of the liver. The leukocytes numbered 10,400 per cubic millimeter of blood and the erythrocytes 5,180,000.

DISCUSSION

DR CARL LAYMON, Minneapolis. The patient's eruption is similar to that of a woman presented as having angioma serpiginosum at a meeting of the Dermatologic Conference of the Mississippi Valley in 1936 (*ARCH DERMAT & SYPH* 35:977 [May] 1937), except that it is much less severe. Although my concept of angioma serpiginosum is not clear, I believe the consensus is that the term should be limited to a nevoid type of telangiectasia, as contrasted with similar conditions of inflammatory nature, such as Schamberg's disease.

DR HAMILTON MONTGOMERY, Rochester. The lesions in the patient with angioma serpiginosum who was presented at that meeting three years ago have faded out. In patients with Schamberg's disease there are cayenne pepper spots, the results of deposits of hemosiderin in the skin, there are no deposits of hemosiderin in those with angioma serpiginosum. Histologically there are a dilatation of blood vessels and a perivascular infiltrate in the upper part of the cutis, some liquefaction necrosis of the basal cell layer and a varying degree of parakeratosis. Sections in this case do not show parakeratosis, but they do show hyperkeratosis. Otherwise the changes are consistent with a diagnosis of angioma serpiginosum. Clinically the condition is not as typical as the one in the case that was previously presented.

DR HENRY E. MICHELSON, Minneapolis. I think Dr Laymon and I agree that purpuric pigmented lichenoid dermatitis is not an entity. We have seen the entire syndrome or parts of the syndrome in many different conditions, such as pityriasis rosea and drug eruptions.

Perforating Gumma of the Soft Palate and Nasal Septum Asymptomatic Neurosyphilis

A white married woman aged 28 came to the clinic in September 1939. She was referred to the Section on Dermatology and Syphilology because of two ulcers, one on the right side of the cartilaginous portion of the nasal septum. For the preceding six months she complained of a stuffy nose, of difficulty in breathing and of a purulent discharge from the nose. One week before she came to the clinic she first noticed an ulceration of the soft palate, which was only slightly tender.

The past history was entirely insignificant. The results of the Kline, Kahn, Hinton and Kolmer tests on the blood serum were as follows: Kline test, 4 plus, Kahn test, 4 plus, Hinton test, positive, and Kolmer test, very strongly positive (44). Examination of specimens of the lesions with dark field illumination did not disclose *Spirochaeta pallida*. The Wassermann and Kline reactions and the results of the Nonne test and the colloidal gold test on the cerebrospinal fluid were as follows: Wassermann reaction, strongly positive, Kline reaction, 4 plus, Nonne test, negative, and colloidal gold curve, 1221000000. The concentration of total protein in the cerebrospinal fluid was 30 mg per 10 cc. Each cubic millimeter of the cerebrospinal fluid contained 34 small lymphocytes. Treatment has not been started.

A Group of Cases of Pyoderma with Various Systemic Manifestations

CASE 1—*Erythema Multiforme? Infectious Eczematoid Dermatitis? Chronic Ulcerative Colitis*

A married woman aged 40 has had active chronic ulcerative colitis for more than two years. Eight years ago the patient had constant diarrhea and bloody stools. The chronic ulcerative colitis has been treated intensively, this treatment has included supportive measures, and two blood transfusions were administered in the last four weeks before the patient was examined in the Section on Dermatology and Syphilology. The patient has been taking various drugs, including barbiturates, acetylsalicylic acid and phenolphthalein. One month ago the patient had a transient attack of urticaria which involved her legs. Three weeks later an eruption appeared on the sides of the neck and on the extensor surfaces of the arms. The eruption consisted of edematous red papules which tended to coalesce in plaques and show a corymbose grouping. In the succeeding days the lesions on the skin became better defined than they had been, and vesiculation occurred in some of the plaques. No lesions were present on the mucous membranes. Serodiagnostic tests did not reveal any evidence of syphilis. Biopsy of a specimen of a lesion disclosed erythema multiforme and dermatitis medicamentosa.

CASE 2—*Pyoderma Chronic Ulcerative Colitis*

A married woman aged 31 had had chronic ulcerative colitis for six years. Clusters of vesicular pustules appear on the skin. The lesions particularly involve the vulva and the adjoining skin of the thigh and abdomen. The individual lesions have coalesced and formed extensive vesicopustular plaques. There is no ulceration. Smaller lesions are on the right flank and in the right axilla. Four years ago the patient had a mild attack of similar lesions which lasted two or three months. Administration of azosulfamide (neoprontosil, disodium 4-sulfamidophenyl-2'-azo-7'-acetyl-amino-1'-hydro-naphthalene-3',6'-disulfonate) and the use of blood transfusions have improved both the colitis and the pyoderma.

CASE 3—*Pyoderma Gangraenosum Chronic Ulcerative Colitis*

A boy aged 14 had chronic ulcerative colitis for two years. He was treated with blood transfusions and injections of Barden's serum. In 1938 he had lobar pneumonia. In January 1939 a crop of pustular lesions appeared on his scalp. The lesions coalesced, and undermining occurred. He has had a gradually descending cellulitis which involves the entire periphery of the scalp. Ulceration is present on the dorsum of the right foot and on the right ankle. The ulceration has the features of pyoderma gangraenosum. For six months before presentation colitis has been rather inactive, but moderate secondary anemia and transient arthralgia have persisted. Treatment has consisted of blood transfusions and dietary measures, including vitamin supplements. Various antiseptic preparations, including a paste of zinc peroxide, have been applied to the ulcers. Azosulfamide (neoprontosil), 35 grains (2.27 Gm) per day, was administered a week ago.

CASE 4—*Pyoderma Gangraenosum of the Neck and Thighs Without Colitis*

The patient is a married woman aged 51. When she came to the clinic a firm nodular subcutaneous swelling was present at the angle of the jaw on the left side.

Below the swelling there was a cluster of inflammatory sinuses which extended forward on the neck. A diagnosis of tuberculosis of the skin had been made before the patient came to the clinic. On the skin of both thighs are impetiginous bullae and ecthymatiform ulcers which appear to spread from day to day by inoculation. On the left forearm there is a scar which was said to be an intense reaction to a tuberculin test.

Various examinations at the clinic, including a study of two histologic sections, did not reveal any evidence of tuberculosis. A bacterial culture produced a pure growth of *Staphylococcus aureus*. The only other abnormality disclosed by physical examination was a moderate degree of secondary anemia. Filtered roentgen rays were applied to the swelling on the jaw on two occasions. The oral administration of acetarsone for one week produced toxic erythema and fever.

CASE 5—*Hidrosadenitis and Pyoderma with Colitis*

A man aged 25 came to the clinic on Sept. 11, 1939, because of an ulcer in the right axilla and one on the right thigh. In March 1938 he sustained a minor abrasion of the right hand. This injury was complicated by mild lymphangitis. Axillary adenitis, systemic symptoms, chills and fever occurred gradually after the injury. The abscess in the axilla was drained but failed to heal. In the summer of 1938 sloughing of the skin of the right axilla occurred after an attack of pneumonia. A few months later skin was obtained from the right thigh and applied to the healing wound in the right axilla. The graft did not take, in fact, peripheral undermining and extensive suppuration occurred both at the site of the graft and in the right thigh. Neoprontosil and sulfanilamide were administered at different intervals for three months, and the patient has received transfusions of blood.

Bacterial culture of both wounds disclosed hemolytic streptococci. The use of various antiseptics, including a paste of zinc peroxide, has produced healing of the ulcers. An attempt has been made to increase the general resistance of the patient by means of a high caloric, high vitamin diet.

DISCUSSION

DR LOUIS A. BRUNSTING, Rochester. There is a variety of ulcerative conditions of the skin which are seen in patients with chronic ulcerative colitis. None of the present group of patients has had the typical characteristics of pyoderma gangraenosum, of which we have observed some 20 cases to date. Erythema multiforme and erythema nodosum are frequently seen with chronic ulcerative colitis. In the entire group secondary anemia and polyarthritides persisted over a long period after the condition in the bowel had subsided.

As far as the treatment of acute pyoderma gangraenosum is concerned, we have found blood transfusions and administration of sulfanilamide derivatives to be of definite value. For the undermined ulcers of this type in which hemolytic streptococci are present we have used Meleney's zinc oxide paste with considerable success. (This paste is made as follows: Bake 40 Gm of zinc peroxide (Merck) for four hours, add 20 cc of glycerin, make up to 200 cc with sterile triple-distilled water, shake well.)

It is risky to traumatize the skin in patients who have chronic ulcerative colitis. The administration of medications or vaccines by hypodermic injection not infrequently leads to the formation of abscesses with ulceration of the skin.

Generalized Erythroderma (Hodgkin's Disease?)

A white man aged 62 came to the clinic because of universal exfoliative dermatitis which was associated with hyperpigmentation and adenopathy. The disease of the skin had remained practically stationary for four months before the patient came to the clinic. During the previous four years he had had occasional attacks of intense pruritus and regional dermatitis, usually lasting several weeks. Examination had disclosed abnormal amounts of arsenic in the urine. Injections of sodium thiosulfate had had no appreciable effect.

Examination of the urine at the clinic did not disclose any arsenic. Microscopic examination of a specimen of skin revealed a nonspecific inflammatory reaction. The erythrocyte count and the value for the hemoglobin were normal. The leukocyte count varied from 10,000 to 16,000 per cubic millimeter. A differential leukocyte count revealed 15 per cent lymphocytes, 6 per cent monocytes, 66 per cent neutrophils and 13 per cent eosinophils. The eosinophils and the toxic changes in the leukocytes were suggestive of Hodgkin's disease. The patient has been observed at the clinic only two weeks. Filtered roentgen rays of moderately high voltage are being applied.

DISCUSSION

DR PAUL A. O'LEARY, Rochester. I classify this type of erythroderma as a lymphoblastoma, considering it as a low grade form of the disease, in which clinical signs of glandular involvement may not appear for several years. When arsenic does not explain the pigmentation, it may be the result of lymphomatous involvement of the chromaffin system. The improvement following systemic roentgen therapy has added to my impression that the patient has a mild type of lymphoma.

DR WALTER POPP, Rochester. This condition is being treated as a lymphoblastoma. Because of the fact that fever, constipation and backache due to involvement of the retroperitoneal lymph nodes in lymphoblastoma are commonly seen, in addition to treatment of the regional nodes, several treatments have been given over the epigastrium. It is assumed that the material relief from a generalized erythroderma can be obtained just as a generalized pruritus complicating a lymphoblastoma can be relieved.

DR HAMILTON MONTGOMERY, Rochester. The histologic picture is that of a generalized neurodermatitis and does not show specific changes for any of the lymphoblastomas. It is true that there is an increase in monocytes. No immature cells are to be found. We have observed several cases of exfoliative dermatitis in association with allergic manifestations in which there was intensive and diffuse generalized pigmentation. Because of the increase in infiltration seen histologically in these cases, systemic roentgen therapy was employed, with benefit.

Senile Pruritus (Neurodermatitis?) Hemangioendothelioma of Left Foot (Kaposi's Sarcoma?)

A man aged 26 has extensive scaling of the entire body. The eruption is moist in the folds of the groins and in the flexures of the extremities. General physical examination does not disclose any abnormality which would account for the dermatitis. The erythrocyte and leukocyte counts and the value for the hemoglobin were normal. The value for the urea was 28 mg per hundred cubic centimeters of blood. The urine did not contain any arsenic. Histologic examination of a specimen of a lesion which was removed from the right forearm disclosed neurodermatitis. The treatment of the pruritus has been symptomatic.

The patient also has a group of small bluish brown tumors of the skin. These are limited to the region of the great toe of the left foot. The patient first noticed these tumors about twelve years before he came to the clinic. They have increased gradually in size but otherwise have not caused any trouble. Examination of the tumors does not disclose any evidence of irritation or ulceration. The microscopic appearance of a section of one of the tumors was consistent with that noted early in the course of Kaposi's sarcoma.

Seborrheic Eczema

A married Negress aged 32 came to the clinic Aug. 18, 1939, because of extensive dermatitis which involved the scalp, ears, neck, axillas and groin. In 1928 she had generalized exfoliative dermatitis following arsenical therapy for syphilis. In 1935, after an infection of the upper part of the respiratory tract, the patient had ulcers in her mouth and an eruption on her face. The micro-

scopic appearance of one of the lymph nodes simulated that seen in cases of Hodgkin's disease, and roentgen therapy was employed. The diagnosis of Hodgkin's disease was later refuted. For the following two or three years the skin has been relatively clear except for the occasional occurrence of an eruption in the groin and aphthous lesions in the mouth.

The present illness began in February 1939, and the severity of the dermatitis has increased progressively. When the patient was first seen at the clinic, examination revealed extensive oozing of the scalp, especially over the occipital region. The oozing was associated with a boggy mass which was suggestive of Celsus' kerion. Repeated examinations of this lesion by microscopic and cultural methods did not disclose any fungi but revealed only *Staphylococcus aureus*. There has been a serosanguineous discharge from the external auditory canals. This has been associated with swelling of the pinna and surrounding tissues.

At first the dermatitis tended to improve, but lately it has spread over the face and has been associated with edema. Inflammatory papules, which have a slight tendency to occur in groups, have spread over the neck, shoulders, arms and legs. A diffuse oozing dermatitis has been present in the axillas and groins. General physical examination did not disclose anything significant, and there is no evidence of diabetes. Urinalysis did not reveal any abnormality. The value for the blood sugar is less than normal. The results of sensitization tests with common foods and pollens were essentially negative, as were the results of cutaneous tests with trichophytin and oidiomycin. Microscopic examination of a specimen of the lesion of the scalp revealed a nonspecific chronic granuloma. The general physical condition of the patient is fair.

DISCUSSION

DR PAUL A. O'LEARY, Rochester. When this patient first came under our observation the mass on the back of the scalp suggested a kerion Celsi, and the cutaneous picture seemed to be that of a trichophytid. Efforts to demonstrate fungi were futile. The cutaneous lesions have changed under several weeks' treatment in the hospital, and today we have made the diagnosis of seborrheic eczema, for want of a better name. The entire process is probably infectious, although therapeutic efforts in that direction have been unsuccessful, owing in a measure to the patient's decided sensitivity to most of the applications tried.

DR LOUIS A. BRUNSTING, Rochester. Boiled milk caused quite a febrile reaction, the temperature rising to 104 F. Since that time extension has been more rapid. She had a history of exfoliative reaction to arsphenamine and cutaneous sensitivity to mercury.

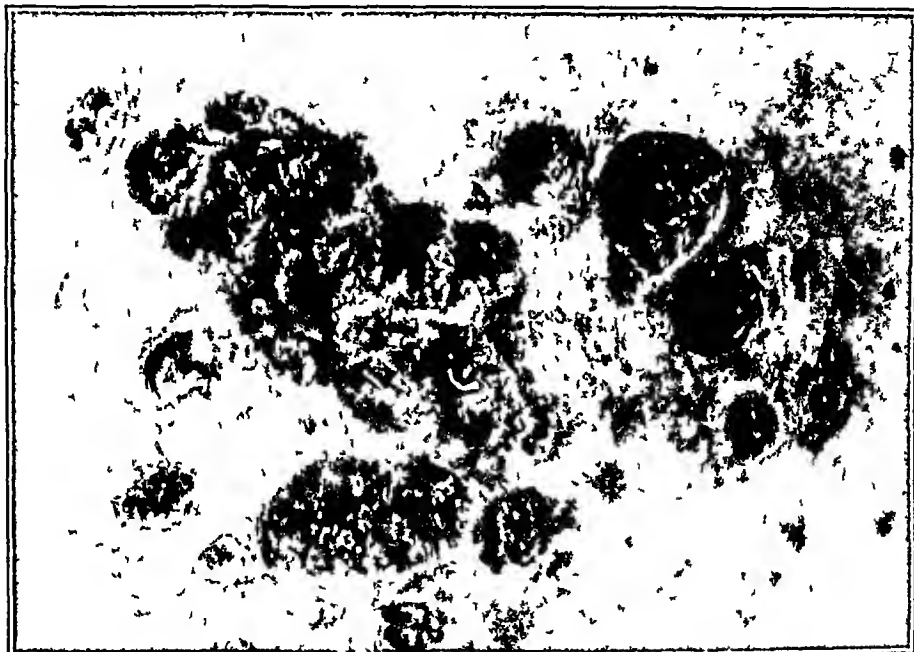
Dermatitis Herpetiformis

A married woman aged 60 came to the clinic because of a universal eruption which has been present for seventeen months. Examination of the skin reveals a polymorphous eruption which is characterized by gyrate inflammatory urticarial lesions, discrete tense bullae and extensive pigmentation. Keratoderma is present on the palms and soles. The mouth has been involved at various times. The oral lesions consist of small vesicles which have a tendency to break down in a short time and form small ulcers. Treatment has included the administration of sulfanilamide, germanin, vitamin concentrates, various forms of arsenic and transfusions of blood. The patient has moderate albuminuria and mild secondary anemia. The leukocyte count was 16,500 per cubic millimeter of blood. A differential blood count disclosed 14 per cent lymphocytes, 6 per cent monocytes, 42.5 per cent neutrophils and 37.5 per cent eosinophils. The disease has the features of erythema multiforme, dermatitis herpetiformis and pemphigus. The results of examination of a histologic section favor a diagnosis of dermatitis herpetiformis.

Hodgkin's Disease, Cutaneous and Glandular

A boy aged 8 came to the clinic in September 1939, because of generalized lymphadenopathy and ulcerating lesions on the thoracic wall. In May 1939 he had first noticed an enlargement of the lymph nodes above the right clavicle. Roentgenologic examination disclosed a large mass in the thorax. Microscopic examination of an enlarged supraclavicular lymph node revealed the presence of Hodgkin's disease. Intensive roentgen therapy was applied to the enlarged lymph nodes and also to the thorax.

During the past five weeks the patient has lost 18 pounds (8.2 Kg). In the past three weeks an intense generalized pruritus has developed. A large tender ulcerating mass has developed on the wall of the left side of the thorax in the



Hodgkin's disease affecting the skin

past six weeks (figure). Histologic examination disclosed evidence of Hodgkin's disease, that is, single multinucleated Sternberg-Reed cells in the necrotic region in the center of the lesion.

E. M. RUSTEN, M.D., *President*

F. W. LYNCH, M.D., *Secretary*

Minneapolis, Dec. 1, 1939

Atopic Dermatitis Presented by DR. S. E. SWEITZER, Minneapolis

L. C., a white man aged 17, first noted an eruption on his face, neck and arms in the spring of 1938. It cleared completely the following summer but recurred in November 1939. Itching is more severe on exposure to wool. He has had severe attacks of poison ivy dermatitis and vasomotor rhinitis each year until 1939.

There is no family history of allergy.

There is an erythematous papulovesicular eruption on the face, neck, extensor surfaces of the arms and back of the left knee. Grouped pollen tests gave negative results.

DISCUSSION

DR. CARL W. LAYMON, Minneapolis Most observers find that the most favorable results in the treatment of atopic dermatitis are obtained through a change of environment, even if it is only the removal of the patient from the home to a hospital. Topical applications and roentgenotherapy perhaps rank next in efficacy. In my experience specific therapy based on the results of cutaneous tests has been most disappointing.

DR. LOUIS A. BRUNSTING, Rochester Atopic dermatitis and conjunctivitis in most cases are made worse by the onset of cold weather, but occasionally the opposite will be true, and it is particularly in cases in which the worst season is during the fall of the year that ragweed pollen may be thought of as a definite factor of aggravation. With patients beyond the age of 7 years cutaneous tests as a rule are of no value for securing clues regarding diet. In cases in which the condition is more advanced treatment is exceedingly difficult unless a change of environment can be effected.

Argyria. Presented by DR. S. E. SWLITZER, Minneapolis

A R., a white woman aged 75, is presented, with a grayish discoloration of the face and neck which developed seven years ago after she had used mild protein silver eye drops for two years.

Since September 1939 she has received weekly treatments of intradermal and subcutaneous injections of a solution of 1 per cent potassium ferricyanide and 6 per cent sodium thiosulfate. She has improved slightly.

There is a grayish tinge to the skin of the face and neck. The conjunctiva is grayish black. The eyegrounds are normal.

DISCUSSION

DR. WILLIAM R. HILL (by invitation), Rochester The clinical picture is typical. The patient has a slate blue discoloration of her face, conjunctiva, external auditory meatus and nails. I noticed in the history no reference to corneal opacities which this woman presents. They are definitely seen and apparently are due to deposition of silver in Descemet's membrane. A slit lamp examination should be made. The patient does not recall past events well. However, at one time she took powders for "stomach trouble," and they may have contained silver. In Dr. Pillsbury's and my series of cases of generalized argyria there was only 1 instance—and this is open to question—in which the condition was due to instillation of solutions containing silver into the conjunctiva. If the condition in this case has occurred from the use of silver in this fashion, it is unique.

Necrobiosis Lipoidica Diabeticorum Presented by DR. S. E. SWETZER, Minneapolis

N. H., a white woman aged 63, has a red lesion on the calf of the right leg which developed three years ago. It has gradually increased in size. She has been treated for diabetes since 1931. She was presented at the meeting on April 14, 1939 (report not published in the transactions). Since then the area has doubled in size.

There is a bright red infiltrated lesion on the calf of the right leg, 8 cm. in size. In the center the epidermis is atrophic, but there is no evidence of ulceration. The lesion is irregularly shaped and has numerous brownish pigmented spots at the periphery.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester Dr. Hildebrand, Dr. Ryncarson and I have recently reviewed all of the cases of necrobiosis reported in the literature, including 8 cases observed at the Mayo Clinic. It is interesting to note that in

a total of 86 cases, 90 per cent of the patients were women and 90 per cent were persons with diabetes, and in 18 per cent of the cases the lesions of necrobiosis occurred from one to five years before symptoms of diabetes developed. In the cases in which diabetes was not found, most of the patients gave a familial history of diabetes or of a high sugar tolerance curve. It is important to distinguish the asymmetric or symmetric, small to large areas of diabetic gangrene, which show little fatty changes in the connective tissue and which present none of the clinical features of necrobiosis lipoidica diabetorum. Necrobiosis histologically is characterized by fatty degeneration of the connective tissues, with extracellular deposits of lipoids, especially in the form of free cholesterol and lecithin. There is a peripheral zone of infiltrate of lymphocytes, leukocytes and histiocytes about the central area of necrobiosis, which may simulate the histologic picture of granuloma annulare. The latter condition shows relatively little deposition of fat. When giant cell reaction occurs in necrobiosis, I believe it is of a foreign body type and has nothing to do with tuberculosis.

DR L. H. WINER, Minneapolis. In view of the presence of fat-staining substance in the connective tissue and the absence of sarcoid type of infiltrate, it is my opinion that the condition is nondiabetic necrobiosis.

DR CARL W. LAYMON, Minneapolis. Oppenheim, in his original discussion concerning the pathogenesis of necrobiosis lipoidica diabetorum, stated the belief that the lipid droplets seen in histologic sections of the lesions were derived from fatty degeneration of the connective tissue. Urbach on the contrary felt that there was an imbibition of lipoids into the tissues from the blood stream. In general, pathologists are loath to admit that a change from proteins to fats, that is, fatty degeneration of proteins, is possible.

In view of our poor therapeutic results in necrobiosis, I was surprised to hear at the recent meeting of the American Academy of Dermatology (*ARCH. DERMAT. & SYPH.*, to be published) that several physicians reported involution of the lesions following extremely heavy doses of ultraviolet irradiation.

Systemic Blastomycosis. Presented by DR S. E. SWETZER, Minneapolis

In H. F., a white man aged 29, a cough developed in October 1938. In January 1939 he began to cough up clots of blood in the morning, and a short time later sharp pains developed in the left shoulder, followed by loss in weight, fever and anorexia. Early in February his ankles became painful, and the right one showed some swelling. On March 1 subcutaneous nodules began to appear. The first of these was on a lower extremity, another appeared just above the right angle of the jaw, and finally they developed over the entire body. In June warty lesions appeared on the nose, upper lip and left eyebrow. The nodules were not painful.

The patient is a pale, emaciated white man. There are numerous subcutaneous nodules over the entire body, especially on the extremities. On the nose and upper lip and over the left eyebrow are verrucous lesions. The liver is enlarged.

Blastomyces dermatitidis was found in wet preparations and in cultures made from many of the lesions. Cultures of the blood and spinal fluid did not show this organism.

Roentgen examination of the lungs showed an area of infiltration in the left apex. Examination of the bones showed rarefaction of the lower dorsal and upper lumbar vertebrae and of the left heel bone.

DISCUSSION

DR LOUIS A. BRUNSTING, Rochester. This case reminds me of one that I observed about twelve years ago. There were ulcerations of both ankles, multiple subcutaneous abscesses and finally metastatic involvement of the liver, lungs and brain. Roentgen therapy was given, and 900 grains (58 Gm.) of potassium iodide a day was administered, without benefit. Once this disease passes the barrier of

a localized infection the prognosis is poor. As a public health measure in cases of this type, when death occurs I recommend that the body be cremated.

DR. HAMILTON MONTGOMERY, Rochester. In the case referred to by Dr. Brunsting, which I reported (*M Clin North America* 14:651, 1930), the patient came to us with a large ulcer of the ankle which had been treated by surgical procedures. A diagnosis of blastomycosis should be dependent on demonstration of budding organisms in potassium hydroxide preparations or in histologic sections of the tissue, as cultures may at times show endosporulation, and thus an erroneous diagnosis of coccidioidal granuloma may be offered. It is important to distinguish between blastomycosis, coccidioidal granuloma, torulosis and various types of so-called South American blastomycosis.

DR. F. T. BECKER (by invitation), Duluth. I have recently observed a case of systemic blastomycosis. There is an excellent review of the literature by Martin and Smith (Martin, D. S., and Smith, D. T. *Am Rev Tuberc* 39:275 [March] 1939). They found a mortality rate of 92 per cent in cases of systemic blastomycosis that had been followed over a period of two years. They have found iodide therapy definitely harmful to allergic patients. The degree of allergy to the infection was determined by performing an intradermal test with a 1 to 1,000 dilution of the blastomycetes cultured on blood agar. If the patient was found to be hyperallergic, desensitization was carried out by increasing the doses of the vaccine. After this procedure iodides could be administered cautiously. I tried this method of treatment in my case, without success.

DR. HENRY E. MICHELSON, Minneapolis. I think that every patient with blastomycosis is more or less a rule unto himself. The strictly localized lesions do fairly well with freezing, some roentgen ray treatment and arsenic taken internally. I do not believe that iodides are of much value, in fact, I doubt if they are of any value. Mutilation often results from excision of the lesions, so I doubt if this is a good form of treatment. In the generalized cases startling results are sometimes seen from the use of trypanamide intravenously, but eventually the patient gets worse, and usually the case terminates fatally. Pathologically the condition is interesting, for acuteness and chronicity exist side by side, so that the immunity of the process cannot be judged from the pathologic observations. I think it is a dangerous disease, and it is too bad that more knowledge concerning its source and treatment is not available.

DR. S. E. SWEITZER, Minneapolis. Dr. Butler mentioned excision of these lesions. Recently I saw a patient with one solitary lesion on leg. A surgeon had twice excised it carefully, but both times it recurred.

Sarcoid of Darier and Roussy. Presented by DR. S. E. SWEITZER, Minneapolis.

E. F., a white woman aged 53, first noticed an erythematous nodular eruption on both knees in August 1939. New lesions of the same nature subsequently appeared on both anterior tibial surfaces a few weeks after the original onset of the eruption and have gradually resolved, so that at present they are invident. The ankles began to swell about two months ago and have caused some pain.

Examination shows a discrete dusky red nodular eruption of six or eight nodules on each knee. The nodules are 1.5 cm in diameter and not tender. There is no tendency toward confluence or ulceration. The ankles are edematous and tender. The Mantoux test gave negative results.

(Histologic sections were shown.)

Besnier-Boeck-Schaumann Disease. Presented by DR. S. E. SWEITZER, Minneapolis.

L. R., a white woman aged 56, noticed a reddish brown lesion twelve years ago on the right leg. It has become gradually larger by peripheral extension. Three years ago other areas developed, and a similar spot appeared on the left leg. Since that time several of the lesions have completely disappeared.

There are many yellow plaques on both legs. The epidermis over these lesions is atrophied, and there is some telangiectasia. The healed areas show epidermal atrophy.

Roentgen examination of the chest gave negative results. The result of a Mantoux test was 4 plus.

A Case for Diagnosis (Sarcoid? Lupus Erythematosus?) Presented by DR PAUL A O'LEARY, DR HAMILTON MONTGOMERY and DR LOUIS A BRUNSTING, Rochester

An unmarried Mexican, an office clerk aged 45, has had a dermatitis of the face continuously for twenty years. He attributes the eruption to long exposure to the sunlight while engaging vigorously in sports over a week end. Within a week the skin had gradually assumed an erythematous appearance, and red papules had studded the face. The eruption has never cleared since the onset, although he has noticed a decided improvement between the months of October and January. The skin of the face is extremely sensitive to sunlight, with visible edema and increased erythema developing after an exposure of only fifteen or twenty minutes. There is no constitutional reaction associated with the photosensitivity, nor does a similar eruption develop on other regions of his body after exposure to the direct rays of the sun. The nose, the lips and the chin have never been implicated in the process.

Aside from a moderate degree of obesity, constipation and dental infection, his health is good. Examination of the blood and of the urine revealed no abnormal findings. The flocculation tests of the blood for syphilis gave negative results. A roentgenogram of the chest showed some torsion of the arch of the aorta and no infiltration in the lung fields. Roentgenograms of the hands showed no abnormality. The basal metabolic rate was -10 per cent. Intradermal tests with purified protein derivative of tuberculin, in both weak and strong concentrations, have yielded negative reactions. There is no family history of tuberculosis, and the patient has had no suspicious tuberculous contacts. He has lived in Mexico, D F, during the past thirty years except for three years which were spent in Tampico, at which time he believes that he improved slightly.

The patient presents a moderate diffuse, doughy infiltration of the face, which is more prominent on the right side of the forehead and the cheeks. On the affected parts is a diffuse, superficially scaling erythema, with numerous scattered pinhead-sized to pea-sized, reddish and yellowish nodules and tiny follicular pustules.

Treatment has consisted of dental extractions and injections of gold sodium thiosulfate intravenously for the past three weeks. The skin has improved materially.

Histologic studies indicate the diagnosis of lupus erythematosus associated with questionable hematogenous tuberculosis, probably of the sarcoid type.

DISCUSSION ON PAPERS OF DR SWEITZER AND DRS O'LEARY, MONTGOMERY AND BRUNSTING

DR L H WINER, Minneapolis. My diagnosis in the first case is sarcoid of Darier and Roussy, the histologic description of which corresponds with the picture of erythema induratum seen here.

DR LOUIS A BRUNSTING, Rochester. The condition appears to be early erythema induratum in the nonulcerative phase.

DR HAMILTON MONTGOMERY, Rochester. The condition in the second case, I believe, is typical of sarcoid of Boeck. In the first case the changes observed histologically seem to be those of a nonspecific type of erythema induratum. I do not believe that the atrophic changes are of material significance, as they may occur in a great many conditions.

Three different specimens for biopsy have been taken from the last patient, and all have shown features suggestive of lupus erythematosus, with two of them

fairly characteristic for this condition. In two of the specimens there were also histologic changes suggestive of sarcoid. I have had the opportunity of seeing 3 patients in whom sarcoid and lupus erythematosus were combined in the same lesion, and when the sarcoid lesions responded to treatment all the features of lupus erythematosus were left. These cases do not necessarily imply that lupus erythematosus is due to tuberculosis but simply present the rare coincidental finding of two diseases at the same time, in the same site and in the same person. We were unable to demonstrate any tubercle bacilli in this patient, and the reactions to tuberculin tests were negative. I believe that this case is one of an atypical, tumid type of lupus erythematosus, with question of sarcoid.

DR H. E. MICHELSON, Minneapolis. I think that the condition in the last case is a difficult one to diagnose. One must consider the lesion as a whole and then its component parts. The entire plaque looks like lupus erythematosus, for there are sharp demarcation, a somewhat elevated border and a change of color at the periphery. Some of the small papules could pass as milium sarcoid, but I saw no lupus nodules. Microscopically, there is an infiltrate made up of different types of cells. Some of the cells resembled those of sarcoid and others seemed to indicate only a banal inflammation. All in all, I presume lupus erythematosus is the best diagnosis.

DR LOUIS A. BRUNSTING, Rochester. There has been improvement recently in the last patient after the intravenous injection of gold sodium thiosulfate. In the past, exposure to direct sunlight has aggravated the eruption. There is pronounced induration of the loose folds of the cheeks at this time, but in the earlier examination the surface changes were interesting, the appearance of tiny brownish red nodules suggesting lupus miliaris disseminatus faciei. The microscopic picture at present indicates the unusual combination of lupus erythematosus with sarcoid. There has been neither fever nor leukopenia and no apparent disturbance of general health. It is probable that the condition is lupus erythematosus disseminatus, in the subacute stage, plus sarcoid.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILOLOGY

E. WILLIAM ABRAMOWITZ, M.D., *President*

LEWIS B. ROBINSON, M.D., *Secretary*

Oct 3, 1939

Arsenical Dermatitis with Pigmentation and Alopecia Presented by DR JESSE A. TOLMACH and DR A. FRANKS (by invitation)

M. H., a woman aged 25, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. In September 1938 the patient was found to have a positive Wassermann reaction of the blood during the course of an examination by a private physician for a vesicular eruption on the hands. Intravenous injections of arsphenamine were begun at weekly intervals. After the second injection, a red raised lesion about the size of a quarter appeared on the flexor surface of the right wrist. After the fifth or sixth injection a circumoral and supraorbital erythematous eruption developed, and the eyebrows began to fall out. After six doses of neoarsphenamine and six doses of a bismuth compound, she was given a rest period of one week, after which another course of treatment with an arsenical compound was begun. After the first injection in this series the eyelids, lips, face, legs and feet became swollen and red, and fever developed. The skin of the soles desquamated. Then a generalized erythematous patchy eruption developed. The patches peeled and turned dark brown, almost

black. The cervical lymph nodes were enlarged. The gums were dark, and the tongue, swollen. Although the patient was ill and the patchy erythematous eruption was present, a second dose of an arsenical was given. She became so much worse that administration of the drug was discontinued, and she was then given eleven doses of a bismuth compound at four day intervals. The scalp, pubic and axillary hair began to fall out about two or three weeks after the last dose of arsphenamine, with resulting total alopecia.

The patient was admitted to Kings County Hospital on March 7, 1939, where she remained under treatment for eleven weeks, with substantial improvement. She was admitted to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on July 31, and since then she has improved somewhat. The pigmentation is not as decided, and a few hairs have appeared on the scalp. Nausea and vomiting developed after an injection of glutathione, and she was hospitalized at the New York Post-Graduate Medical School and Hospital on August 26 and was discharged on August 31, improved. Subsequent treatment has consisted only of injections of sodium thiosulfate and liver extract.

Urinalysis showed 20 pus cells per high power field, but the results were otherwise normal. No arsenic was found in the urine. The basal metabolic rate was -16 per cent. The complete blood count was within normal limits. Histologic examination showed a thin epidermis with a large amount of yellowish pigment in the basal cell layer. In the upper part of the corium there were numerous clumps of yellowish to brown pigment in an edematous stroma. The cellular reaction was slight. There was melanin in the upper part of the cutis and in the epidermis. There were granules in the lower part of the epidermis, as seen in arsenical pigmentation. The Perl stain for pigment containing iron was negative. A bleach for melanin gave positive results.

DISCUSSION

DR ISIDORE ROSEN Eruptions and sequelae of this kind are occasionally seen after administration of drugs other than arsenic. In this instance cutaneous manifestations developed after the patient had received a few injections, which should have been a warning against further treatment with the arsenicals. There is no question in my mind but that the condition is the end result of an arsphenamine dermatitis.

DR DAVID BLOOM The total alopecia in this patient seems to me not the form of alopecia which one sees during arsphenamine dermatitis and which is due to the direct action of the arsenic on the skin and its appendages. In this case the alopecia should be considered as probably due indirectly to the action of the arsenic on the endocrine glands or on the sympathetic nervous system, on which growth of hair depends.

DR EUGENE F. TRAUB Some years ago at the International Congress in Copenhagen, Denmark, one of the members of this section reported a series of cases of alopecia (in some the loss of hair was partial and in others total) in which the condition was cured or improved after the use of sodium thiosulfate. Presumably the patients all had a high lead or arsenic content in the blood and urine. As there was a physician in Massachusetts at about the same time who had reported a series of 2,000 cases of chronic lead poisoning, I wrote to him and found that in none of his cases had alopecia been observed. In the patient presented by Dr. Tolmach the alopecia is similar to that seen in 2 or 3 of our patients, all of whom had had a severe cutaneous reaction following arsenic therapy for syphilis. In our cases the hair was restored completely after a number of years of treatment or with little or no local treatment. In all probability hair will be restored in this case, although it is impossible to state this with certainty. It is interesting to speculate on the exact mechanism of alopecia in these cases.

DR FRANK C. COMBES This case illustrates a point brought up by Dr. Osborne (*ARCH. DERMAT. & SYPH.* 18:37 [July] 1928) several years ago on the difference between the action of trivalent and that of pentavalent arsenic. The reticulated pigmentation on the cheeks corresponds well with the arteriole dis-

tribution Osborne, in a microchemical study, showed that the bulk of trivalent arsenic is deposited in the corium around the arterioles and capillaries

DR CHARLES WOLF It might be of interest to know the basal metabolic rate of this patient at the present time I believe that her sympathetic nervous system was damaged to a certain degree by the toxic state which developed, and although the alopecia may eventually disappear, it may also be permanent Endocrine or vitamin therapy might result in restoration of the hair I should investigate her endocrine status and also give her a high vitamin diet and general tonic treatment In other words, I do not believe in letting nature do all the rehabilitation I do not know how much damage was done by the arsenic and perhaps also by the bismuth She told me that she had a blue line on the gums, so she may have a combination of arsenical and bismuth toxic effect

DR HERMAN GOODMAN I should like to ask Dr Traub whether the patients in his series were males or females and whether they had a residual alopecia

DR EUGENE F TRAUB Our patients were all females, and the alopecia of the scalp was total in all of them

DR E WILLIAM ABRAMOWITZ According to this patient's history the basal metabolic rate was -16 per cent

DR CHARLES WOLF Under those circumstances my suggestion to give the patient pituitary and thyroid extracts is in order I believe that she would be helped considerably

DR E WILLIAM ABRAMOWITZ It was stated in the histologic report that melanin was found in the section Would Dr Peck care to discuss that aspect of the subject?

DR SAMUEL M PECK Melanin can be recognized by the experienced histopathologist in unstained sections by its distribution and general appearance The test for iron will rule out the question of blood pigment The melanin itself can be accentuated by means of silver nitrate stain Patients who have a tendency to intense pigment formation, especially Negroes, often increase their normal pigment formation in the process of regeneration If the inflammatory reaction in the melanoblasts is pronounced, there is a tendency for the pigment to be dropped below the epidermis instead of being carried upward and discarded with the scales If the pigment is deposited to a great extent, the condition may be a form of auto-tattooing, which is sometimes observed in lichen planus after the injection of arsenic and the application of roentgen rays

DR HERMAN GOODMAN Are the explanation given by Dr Peck and the discussion by Dr Combes in accord? Doesn't it make any difference whether the arsenic which caused this patient's pigmentation was trivalent or pentavalent?

DR MAX SCHEER It was stated that the pigmentation in this case was due to the pentavalent arsenical, with the presumption that pigmentation of this type does not occur with the trivalent arsenicals Either kind of arsenic can produce a pigmentation of this kind Some years ago I had a case of an irregular pigmentation in a woman who had had psoriasis years before and who had taken solution of potassium arsenite (Fowler's solution) for a long time She had on her back the same type of reticulated pigmentation that this patient tonight shows on the face Therefore, it is the arsenic itself and not the kind of arsenic which is significant

Lichen Planus Following Gold Therapy Presented by DR EUGENE F TRAUB

B K, a woman aged 37, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital The patient now presents a generalized eruption of a few months' duration which consists of irregularly shaped, large and small patches formed by the confluence of small erythematous papules The papules tend to be flat topped and shiny, but many of the patches exhibit moderately fine scaling There is a white striation on the mucous mem-

branes of the mouth, and the tongue is covered by discrete to confluent white flat-topped papules. On both feet there are bullae, those on the soles being rather deeply seated and yellow.

DISCUSSION

DR EUGENE F. TRAUB. Perhaps this case should have been reported as one for diagnosis rather than as a case of lichen planus following gold therapy, because I am unable to prove whether the gold compound the patient received was responsible for the present eruption. The patient had a previous attack of typical lichen planus eight years ago, for which she was treated at the same hospital. A short time ago, after the earlier eruption had completely disappeared, she was given injections of a gold compound for arthritis. The present eruption appeared after the second or third injection. The appearance of the eruption on the skin, buccal mucosa and tongue was rather typical of lichen planus. It is possible that she has an ordinary lichen planus which is in no way related to the gold therapy. On the other hand, it may be more than just a coincidence that the eruption appeared after the second or third injection of the gold compound. A piece of tissue removed for histologic study was reported to show a lichen-planus-like eruption in a case of gold dermatitis. Apparently the pathologist felt that he was able to state that the gold was responsible for the lichen planus. I believe that it would be interesting to have this point discussed more fully.

DR MAURICE J. COSTELLO. About a year ago I presented at the Manhattan Dermatologic Society (*ARCH. DERMAT. & SYPH.* 37:905 [May] 1938) a patient who had vitiligo and who was treated with gold sodium thiosulfate intravenously. The condition was definitely improved by the treatment, but after the ninth injection an eruption developed in the vitiliginous areas which was indistinguishable from lichen planus. She also had lesions in the mouth. Another patient with vitiligo who was treated with injections of a gold compound presented a similar eruption. The toxic manifestations of gold salts given parenterally are not limited to cutaneous reactions. Recently I had occasion to observe a patient who was treated for arthritis by three large doses of gold salts. She subsequently died. I am inclined to believe that larger doses of gold are given by physicians other than dermatologists. A warning should be given to those who use large doses of gold salts, especially in the treatment of arthritis. Fifty milligrams of gold sodium thiosulfate, given intravenously, should never be exceeded. I believe that the lichenoid eruption presented by this patient is due to the toxic effects of gold salts given to her for the relief of her arthritis.

DR FRANK C. COMBES. I should like to repeat Dr. Traub's question and ask some one experienced in histopathology whether it is possible for one not knowing the history of a case to distinguish histologically between true lichen planus and the lichen planus that supposedly follows administration of a gold compound or of arsphenamine?

DR WILBERT SACHS (by invitation). It is my understanding that lichen planus, whether it follows exposure to sunlight or administration of gold or arsphenamine, is just lichen planus. However, it may be possible to make some suggestion as to the toxic process going on in addition to the lichen planus by studying the changes in the blood vessels and noting the large number of wandering connective tissue cells of the type one finds in a toxic process. I think that such a diagnosis can be made on the appearance of the microscopic picture.

DR SAMUEL M. PECK. It is important to know whether the lichenoid eruptions that appear on the skin after treatment with drugs also occur on the mucous membranes. Dr. Satenstein has always maintained that the lichen-planus-like eruptions due to drugs can be differentiated histologically from the true lichen planus by the increased depth of the infiltration of the former.

DR HERMAN GOODMAN. May I ask what the diagnosis would be for the eruption on the abdomen if this woman had no lichen planus or lichen-planus-like eruption? Since the patient was in the hospital some eight years ago for an

eruption that was diagnosed lichen planus, might not the lesions in the mouth be residuals of eight years' duration, and might not the patient have two dermatologic conditions at the present time?

DR EUGENE F TRAUB The gold therapy may have precipitated this eruption. The fact that the patient once had a typical lichen planus which did not follow any type of medication and the fact that it is known that this eruption may recur make it possible that the present eruption might have appeared coincidentally with the gold treatments. It is conceivable, however, that in a patient who is susceptible to lichen planus, gold therapy, which is known to produce lichen-planus-like eruptions, could have at least precipitated the present attack. The facts that the eruption is fading rapidly with the cessation of treatment and that the process in the mouth began as an acute stomatitis which is now resolving into an eruption that could be mistaken for lichen planus suggest that the gold compound was the cause. The present attack is a new one, not a flare-up of a preexisting eruption. I repeat that the report of the histologic examination also seems to confirm the fact that the condition is lichen planus precipitated by gold.

DR LEWIS B ROBINSON In the cases of eruptions due to gold compounds, many of the patients have a preliminary loss of the sense of taste and many have sore mouths. In this particular case the condition in the mouth may simply be a representation of the sore mouth which has assumed the appearance of lichen planus, and the rest of the eruption may be a gold dermatitis.

A Case for Diagnosis (Drug Eruption? Lichen Planus? Pityriasis Lichenoides et Varioliformis Acuta?) Presented by DR SAMUEL FELDMAN

M L, a woman aged 30, was referred to the department of syphilology of the Morrisania City Hospital from the antepartum clinic in May 1939. She was at that time in her third month of pregnancy. She said she had not had syphilis and had never had a sore or an eruption. However, a routine examination of her blood showed a 3 plus Wassermann reaction. She has never had any miscarriages. Her only child, a boy 6 years old, is alive and well, and her husband is in good health. The Wassermann reactions of both husband and son were negative. Examinations of the patient's blood and urine were otherwise normal. The Wassermann reactions on two occasions in June were 2 plus and 3 plus.

Because of the poor condition of the patient's veins, she was unable to receive intravenous injections, and she was therefore treated with bismarsen intramuscularly. The dose administered was 0.2 Gm, twice a week for four consecutive weeks. After that her skin began to itch, and an eruption developed on the chest and the back. Arsenical medication was discontinued, and bismuth subsalicylate was substituted. With the change in treatment the eruption did not diminish in severity or extent. On the contrary, new crops appeared, involving new regions, until the eruption extended over almost the entire body. On the lower extremities, however, it was somewhat sparse. The lesions consisted of small papules, with an occasional larger lesion which was scaly in the center, the appearance was not unlike that of follicular pityriasis rosea. However, the lesions have undergone a gradual change and now present the following picture. There are numerous papules, not larger than a pinhead, some are globular, while others are flat, angular and shiny. There are numerous larger lesions about 0.5 cm in diameter, some of which have a decidedly depressed, often scaly center, while in other lesions the center consists of a brown necrotic crust. No vesicles have been observed at any time. A few days ago some lesions appeared in the mouth which are suggestive of lichen planus.

DISCUSSION

DR PAUL GROSS As far as I understand it, Dr Feldman did not consider the diagnosis of pityriasis lichenoides et varioliformis but rather at first thought of pityriasis rosea. Lichen planus not infrequently resembles pityriasis rosea at the onset.

DR LEO SPIEGEL This case is similar to one I presented about a year ago (ARCH DERMAT & SYPH 38 470 [Sept] 1938) My patient was being treated for early syphilis He had a pronounced secondary eruption and a positive Wassermann reaction After therapy the eruption disappeared, and while he was being treated a pityriasis-rosea-like eruption developed After a number of weeks, the eruption changed, and when he was presented before this section the consensus was that the condition was lichen planus The patient shown tonight presents a similar picture As Dr Feldman said, at first the condition looked like pityriasis rosea This occurrence seems to be frequent after the administration of arsenicals Subsequently the eruption changes and is diagnosed as lichen planus The lesions on the forearms and wrists of this patient are lesions of lichen planus

DR ADOLPH ROSTENBERG I have also observed a similar case When the patient, a man, came to me at first he presented a typical eruption of lichen planus I gave him solution of potassium arsenite (Fowler's solution), and a few weeks later the lichen planus eruption seemed to disappear completely, in its stead I saw a typical eruption of pityriasis rosea I was puzzled and thought I had made an error in my original diagnosis But when the pityriasis rosea disappeared, the lichen planus eruption returned Therefore, I believe that the arsenic produced the eruption that looked like pityriasis rosea and that the lichen planus was the original eruption I believe that the condition in this case is similar a toxic eruption occurring on top of a lichen planus eruption

DR ISIDORE ROSEN A clinical diagnosis in this case would be difficult if the lesions were not studied carefully The first impression is that of an eczema, but on closer inspection one can readily recognize pinhead-sized lichen-planus-like papules The question arises whether the condition is really lichen planus or whether it is a lichen-planus-like eruption, which is occasionally seen after the administration of the arsenicals Histologic examination will establish this

DR EUGENE F TRAUB As so many cases of an eruption that is apparently lichen planus following some type of therapy are being presented, I suggest that the presentation of them be made in a more or less uniform manner For example, this case was of lichen planus following the use of bismarsen, and my case was one of lichen planus following gold therapy My suggestion is that the conditions be labeled, for instance, lichen planus following gold therapy I think this should be done until such a time when it can be proved absolutely that the therapy was responsible for the eruption and not just a coincidental factor

DR E WILLIAM ABRAMOWITZ It is of interest that at the last two meetings a group of cases should be reported with this condition appearing after the administration of arsenic and of gold compounds The literature on eruptions from heavy metals mentions a pityriasis-rosea-like eruption and a lichen-planus-like eruption There is considerable discussion as to whether the conditions are actually lichen planus or only lichen-planus-like The evolution of the various types of eruption, from exfoliative dermatitis to lichen planus and from pityriasis rosea to lichen planus, has also been described In this connection Dr Rostenberg's description of a case in which the eruption changed from lichen planus to pityriasis rosea and back to lichen planus again was interesting The pityriasis-rosea-like eruption is mainly reported as due to bismuth, whereas the lichen-planus-like eruption has been mostly reported as caused by arsenicals and gold I agree with Dr Traub that there should be some uniformity in reporting these cases The question of whether the condition in the case presented is lichen planus or a lichen-planus-like eruption due to a drug cannot of course be settled at present It is known that when a patient has had lichen planus, sometimes there is a recurrence many years later

DR SAMUEL FELDMAN As far as the question of syphilis is concerned, if the patient were not pregnant I should have studied the case longer before instituting treatment I had to treat her immediately because of the pregnancy As to the eruption, I cannot make up my mind that it is a true lichen planus, because I have not seen a true lichen planus with necrotic lesions such as she shows

A Case for Diagnosis (Tertiary Syphilis? Moniliasis?) Presented by DR ANTHONY C CIPOLLARO

G H, a man aged 53, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He had syphilis about twenty years ago, for which he received treatment. About four years ago the present eruption began on the lip, and gradually it spread to the chin. He has received different types of treatment, without any appreciable benefit, although during the past six weeks there has been some improvement as a result of four injections of a bismuth compound.

Examination shows erythema and edema of the lip and chin. There are small indentations (verruculate scarring) not only of the chin but also of the mucous membrane surface of the lower lip. On the dorsum of the tongue are white patches, not unlike those seen in cases of moniliasis.

The Wassermann reaction of the blood and that of the spinal fluid were negative. The colloidal gold curve of the spinal fluid was normal. Urinalysis gave normal results. Examinations for fungi, by both microscopic and cultural methods, failed to reveal any. Histologic examination showed a superficial dermatitis with a cellular infiltration, predominantly of plasma cells. The epidermis was acanthotic. The granular layer was absent. The basal border was intact. Throughout the upper part of the corium there was an extensive and diffuse infiltration composed mainly of plasma cells. There was considerable edema in the subepidermal zone. The collagen bundles in the middle and lower parts of the corium showed parenchymatous edema.

DISCUSSION

DR LOUIS TULIPAN. I think that this man has chronic lymphedema or elephantiasis nostras, such as is so often seen on the legs. He has edema of the lip and small vegetative lesions below the lip. I believe that the eruption has little to do with the syphilis at present but is due to a chronic inflammatory process with lymph stasis and lymphedema plus vegetations on the skin, such as are seen occasionally in lymphedema.

DR FRANK C COMBES. I agree with Dr Tulipan. This man probably had a syphilitic lymphangitis. Now he has an occlusion of the lymph vessels with solid edema of the lip. I do not believe that the lesions on the cheek and tongue are characteristic of leukoplakia.

DR MAX SCHEER. One must make a diagnosis of some sort, and the diagnosis that suggests itself to me is a tertiary hypertrophic hyperkeratotic syphiloderm. Of course, this is a rare syphiloderm. The ones I have seen have occurred on the plantar surfaces and sides of feet in which there were decided keratoses. This is the first time I have seen such lesions on any other part of the skin. With the history and other factors taken into consideration, I think this is the correct diagnosis. It is borne out by the improvement which occurred after four injections of a bismuth compound. Unfortunately bismuth therapy was stopped, and improvement stopped also. I recommend a course of treatment with bismuth compounds and iodides.

DR WILBERT SACHS (by invitation). The biopsy section showed a superficial dermatitis with a contact dermatitis on top of it, with a large number of plasma cells in the cellular infiltrate. There was no suggestion of tuberculosis in the section. It is possible, I think, that the large number of plasma cells may be due to some type of "id" and not to syphilis.

DR HERMAN GOODMAN. This case is practically a counterpart of one I saw years ago. Dr Williams thought that the condition might be esthiomene with blockage of the lymph vessels, that it was syphilitic and that it was on the lip rather than on the genitalia as with textbook esthiomene. The term esthiomene is used in this case to indicate not the named disease but an ulcerative granuloma and lymph stasis. The man had a tremendous edema of the lower lip, with

fungating lesions beneath. The only therapy that seemed to be successful was antisyphilitic treatment, in particular with iodides.

DR DAVID BLOOM. I wonder if Dr Cipollaro considered another diagnosis, namely, sycosis. The vegetations on the chin and also the presence of a large number of plasma cells would fit in with such a diagnosis. The lymphedema of the lower lip could also be explained by the blockage of the lymphatics due to the inflammation produced by the pyogenic cocci. Although the destruction of one ala nasi would suggest the possibility of a syphilitic infection, I should not consider syphilis as a causative factor in the production of the lesion on the chin and lower lip.

DR MAURICE J. COSTELLO. I should like to add another possible diagnosis. The man stated that his eruption was precipitated by sunlight. The eruption was definitely improved after four injections of a bismuth compound. Since lupus erythematosus frequently improves after bismuth therapy and since the original eruption on the lip was not unlike lupus erythematosus clinically, I suggest it as a possible diagnosis and recommend that the patient be given gold salts intravenously.

DR SAMUEL FELDMAN. I want to correct a misconception about the lesion on the nose. The patient said that it was due to a gunshot wound.

Infectious Eczematoid Dermatitis. Presented by DR FRANK C. COMBES

Y. K., an unmarried housewife aged 42, is presented from Bellevue Hospital. Her eruption consists of generalized fairly well defined moist lesions covered with seropurulent crusts and scales. The eruption has a predilection for the neck, chest, scalp, genitalia, ears and eyelids. There are many isolated and grouped follicular pustules. She complains of moderate pruritus. The eruption is of one year's duration, with periods of temporary improvement after various types of treatment. The patient's father died of diabetes mellitus, and her mother died of "heart trouble."

Examination of the blood gave normal results except for evidence of secondary anemia. The urinalysis revealed nothing abnormal except clumps of pus cells. Scrapings from the lesions showed staphylococci but no fungi. Roentgenograms of the chest and of the sinuses were normal.

Treatment has consisted of a high vitamin diet and local use of aqueous solution of brilliant green (tetraethyldiaminotriphenylmethane sulfate) (0.5 per cent), paste of zinc oxide (plain), boric acid ointment, sulfur ointment (40 per cent) and solution of boric acid and resorcinol (2 per cent), as well as roentgen therapy (six doses, each of 75 r). The best results followed roentgen therapy.

DISCUSSION

DR HENRY D. NILES. At present, I think that the only possible diagnosis is seborrheic eczema. I believe the patient said that the eruption started on the umbilicus. There was no focus of infection or draining sinus, which one would expect with infectious eczematoid dermatitis; she has a seborrheic eruption on the scalp, and the eruption has a predilection for the seborrheic areas. One method of treatment not mentioned in the history which has had some success in cases of conditions like this is the use of a 1 or 2 per cent solution of gentian violet in K-Y lubricating jelly. This drug appears more effective in K-Y lubricating jelly than in aqueous or alcoholic solution or in other ointments.

DR CHARLES WOLF. This woman was a patient at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital ten years ago, and at that time she had a solitary lesion on the nasolabial fold, for which I gave her roentgen ray therapy. The condition cleared up temporarily. At that time the diagnosis was seborrheic eczema, and that lesion was the only one. Tonight she gives me the impression of having another disease, moniliasis. She has many lesions that could well fit into that picture, and I suggest studies with that diagnosis in mind.

DR E WILLIAM ABRAMOWITZ Scrapings from the lesions revealed staphylococci but no fungi

DR DAVID BLOOM I had occasion to observe this patient while she was at the Skin and Cancer Unit, and her eruption was always conspicuous because of an exudation of brownish serum in the lesions on the scalp, neck, ears and genital region. This fact suggested a streptococcic rather than a staphylococcic infection. The condition was diagnosed as infectious eczematoid dermatitis, and 30 per cent sulfur in petrolatum was prescribed, which improved the condition considerably but did not clear it up entirely.

DR E WILLIAM ABRAMOWITZ Since I have been administering concentrated (30 per cent) sulfur in petrolatum, I have been particularly interested in differentiating eruptions which are ordinarily called seborrheic eczema from those of infectious eczematoid dermatitis. The latter often appear in the seborrheic areas. There was a report from the Mayo Clinic of a case in which eruptions began about the ears and spread to other parts in which streptococci and staphylococci were found (*J A M A* 113:641 [Aug 19] 1939). From the clinical standpoint the causative factor in producing the dermatosis could not be determined. The earlier report of Mitchell is also appropriate (*J A M A* 108:361 [Jan 30] 1937). I was treating a woman who had a severe generalized eczematous eruption which started behind the ears and spread to the scalp, the folds of the breasts, the groins and the pubic region. I obtained about 50 per cent improvement with the 30 per cent sulfur, but new pustular lesions appeared. She also required treatment for a purulent vaginal discharge. I stopped the applications of sulfur and gave her sulfanilamide, 40 to 50 grams (26 to 32 Gm) a day. The eruption was almost entirely gone by the end of the week, but administration of the drug had to be stopped, for she acquired a toxic eruption from the sulfanilamide and a sore throat (agranulocytosis). The eruption then began to return. I then began the use of ammoniated mercury ointment. Its results were better than those obtained with sulfur and almost as good as those observed with the sulfanilamide. In other words, I believe that this condition is a staphylococcic or streptococcic infection of the skin.

DR MAURICE J COSTELLO I had an opportunity to observe this patient at Bellevue Hospital for two months. She had a fair trial with sulfanilamide and sulfapyridine, with no beneficial effect on the eruption. Improvement followed the application of a 5 per cent aqueous solution of brilliant green tetraethylidiammotriphenylmethane sulfate) and paste of zinc oxide.

DR LEWIS B ROBINSON I should like to report a similar experience. Many kinds of treatment had been tried in my case, with no results. I decided that turkish baths and cleanliness might be of some benefit and prescribed three baths a week. The eruption in the past three months has practically all cleared, so that I am inclined to think that sometimes cleanliness itself is enough.

DR FRANK C COMBES Cleanliness does help a lot of these puzzling dermatoses. Undoubtedly this woman is sensitive to some type of bacteria, cultures will be made of scrapings from her nose and skin. She has a seborrhea, but I take exception to the diagnosis of seborrheic eczema. It is true that the eruption involves primarily the so-called seborrheic areas, but there are other eruptions, particularly moniliasis, that have a predilection for those areas. She showed some temporary improvement with sulfur therapy. Dr Costello has said she improved with brilliant green. I think she responded best to roentgen therapy. She has always improved temporarily with any treatment, only to relapse.

A Case for Diagnosis (Atrophic Glossitis?) Presented by DR HENRY D NILES

L G, a woman aged 26, was seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on June 15, 1939, complaining of a

burning sensation and lesions on the dorsum of her tongue of at least seven years' duration. Her mother has had a similar condition for at least twelve years. The maternal grandmother is reported to have had a similar condition on the tongue. The patient's father and sister are normal.

The patient complains of an occasional burning sensation and patches on the dorsum of the tongue and small lesions on the buccal mucous membrane. The condition remained unchanged after the patient stopped smoking for eighteen months. The burning sensation in the mouth began before any lesions were seen. The tongue always feels dry and is irritated by hot liquids. Her diet is adequate.

Examination shows on each side of the dorsum of the tongue an oval, somewhat shiny, flat grayish atrophic patch devoid of papillae. The patches are not infiltrated. There are no other lesions in the mouth. The teeth are well formed and have no rough edges. There are only amalgam fillings.

Several Wassermann tests of the blood, the last one on July 6, have given negative results. A blood count on July 6 showed 82 per cent hemoglobin and 4,130,000 red cells per cubic millimeter.

The patient has been given many topical applications, roentgen ray treatments, dilute hydrochloric acid, vitamin tablets and nicotinic acid (50 mg twice a day), without improvement in the feeling or appearance of the tongue.

DISCUSSION

DR EUGENE F. TRAUB: Among the congenital anomalies, various types of atrophy have been described, and although I must admit that I have never seen the familial type of atrophy of the tongue, I see no reason why the condition in this patient would not fit into such a category. The girl's mother had a type of atrophy somewhat similar to that shown by the patient. In addition to the atrophic condition, she had a pigmented spot on the lateral side of the tongue which might have been some type of nevus or congenital anomaly. This, together with the fact that the grandmother was similarly affected, certainly suggests a hereditary type of congenital anomaly, presenting the appearance of an atrophic glossitis.

DR DAVID BLOOM: Siemens of Leyden, who has done much work on hereditary conditions of the skin, has mentioned certain conditions of the tongue as hereditary but not this type of atrophy. It is of great interest to have on record this condition occurring in daughter, mother and possibly grandmother.

DR ADOLPH ROSTENBERG: This patient reminded me that she had been to see me about ten years ago. As I remember, she had practically the same condition then that she has now. I believe that it is congenital and that some one called her attention to it and she is frightened. Subjective symptoms are slight and of a functional nature. I should not treat her at all, as treatment would only aggravate the condition and not cure it.

DR HERMAN GOODMAN: The malady probably has occurred in the mother, grandmother and daughter, but perhaps the conditions under which they live have something to do with it. Each one not only shows a smooth tongue but also complains of a burning sensation of the tongue.

DR LOUIS TULIPAN: I believe that there is a condition described as superficial smooth atrophy of the tongue (Hazen, H. H. *Atrophy of Mucous Membranes*, *J. Cutan. Dis.* 34: 801 [Nov] 1916). This girl has atrophy, and I believe it comes under this heading.

DR HENRY D. NILES: I also considered lichen planus. I have examined the patient several times but have seen no lesions on her integument or on the buccal mucosa. One cannot ignore the family history. The mother has definite changes on the tongue, although they are not as conspicuous as those on the daughter's tongue. I neglected to mention the question of diet and vitamin deficiency. I investigated this point and found that the patient has a definitely adequate diet, as has the mother. I felt, as some of the speakers did, that the condition was no doubt congenital and hereditary and probably of no importance. I considered that it

would be good psychotherapy to present the patient here and to tell her later the opinion of this section. She has no cancerphobia, as one might expect in such a case.

Leukoderma Acquisatum Centrifugum (Sutton). Presented by DR DAVID BLOOM

B C, a girl aged 15, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, complaining of an eruption on the face of two years' duration. On both cheeks are several round depigmented lesions, of which one shows a central pinhead-sized pigmented spot and two surround a lentil-sized raised pigmented nevus. Near the right angle of the mouth is a pea-sized slightly depigmented area without any central pigmented spot or nevus. One nevus appeared two years ago, shortly before the depigmentation developed.

The patient has had two treatments with a quartz mercury vapor glow lamp following the application of oil of bergamot.

DISCUSSION

DR SAMUEL FELDMAN: Why use the name *leukoderma centrifugum acquisitum*, when the condition is not centrifugal or acquired? It is a nevus and always has been. Why not call it a nevus?

DR HERMAN GOODMAN: The name should be *perinevoid vitiligo*. There are two types: one which begins as a black spot, with the white area appearing around it, and the other which begins as a white ring, with the black spot appearing in it later. There is no way to distinguish one from the other. I watched one boy for many months and never saw any change. There is a beautiful picture of this condition in Sutton's book (Sutton, R. L. *Diseases of the Skin*, St. Louis, C. V. Mosby Company, 1928, p. 633).

DR DAVID BLOOM: I am inclined to agree with Dr. Feldman in regard to the best name for this type of lesion. I also believe that the depigmentation is *nevroid* and that the name should express it. However, I did not feel that I should use another name, as long as no term has been settled by the authorities.

DR SAMUEL FELDMAN: In a paper read some years ago (*ARCH. DERMAT. & SYPH.* 34:590 [Oct.] 1936), I presented cases in every one of which there was a dark spot. The depigmented area was in 1 case a true anemic nevus. Whether the white areas appear afterward, are concurrent or appear before, the nevus are of two types: the single spot, which is a real nevus with nevus cells, and the white area, in which the pigment is completely lacking.

LOS ANGELES DERMATOLOGICAL SOCIETY

CHRIS HALIORAN, M.D., *Chairman*

SAUL S. ROBINSON, M.D., *Secretary*

Oct. 10, 1939

Lupus Erythematosus Involving the Lips Addison's Disease? Presented by DR SAUL S. ROBINSON

J. P., an unmarried Negress aged 37, states that about two years ago an eruption developed on the lips. Subsequently the neck, the upper part of the back, the preauricular regions and the upper part of the thorax became involved. There have been periodic improvement and exacerbation, the latter occurring at

the time of the menses Exposure to sunlight makes the eruption worse There is a history of healed fibroid pulmonary tuberculosis in 1925 and lupus vulgaris (?) of the face in 1927

The patient is poorly developed and poorly nourished and is of the asthenic type There is a generalized yellowish brown pigmentation involving the buccal mucosa The lips show scaling, atrophic brownish red plaques, with punctate scarring

A blood count revealed 74 per cent hemoglobin, 4,180,000 erythrocytes per cubic millimeter, 12,000 leukocytes per cubic millimeter, 70 per cent polymorphonuclear neutrophils, 20.5 per cent lymphocytes and 9 per cent monocytes The Wassermann and Kahn reactions of the blood were negative The sputum examination revealed no tubercle bacilli The urinalysis was normal

An improvement in the lesions followed the administration of sodium iodobismuthite

DISCUSSION

DR ARTHUR FLETCHER HALL, JR I agree with the diagnosis of lupus erythematosus involving the lips, but I do not suspect the presence of Addison's disease

DR WILLIAM H GOECKERMAN The condition impressed me as a Sencar-Usher syndrome This particular type of eruption is being discussed as lupus erythematosus or pemphigus In my opinion it is a vesiculobullous lupus erythematosus

DR MAX J WOLFF I thought that the condition was lupus erythematosus of the skin and mucous membranes

DR H SUTHERLAND CAMPBELL I do not think Addison's disease is the diagnosis The patient seems to have a rather vivacious character, while lassitude is the rule in Addison's disease

DR SAUL S ROBINSON This patient has been seen by different physicians in the past years, and they have always remarked about the peculiar pigmentation A physical examination in the clinic showed low blood pressure and weakness

Pachyonychia Congenita Dermatitis of the Hands Presented by DR C RUSSELL ANDERSON

Mrs B R, an American nurse aged 57, complains that for seventeen years all the nails of the fingers and toes have been thickened, striated and discolored The nails are so hard that she experiences difficulty in trimming them For twelve years she has had horny papules on the plantar surface of the feet The papules first appeared after the beginning of her occupation as a nurse, with its long hours of standing At times the papules become painful, and she digs out the horny plugs The patient was first seen on Aug 29, 1939, when she presented an acute dermatitis of the face, neck, hands and forearms Ten days ago there was a recurrence of the dermatitis after the use of mazon ointment (a proprietary preparation containing a coal tar distillate and zinc oxide) One daughter has similar changes in the nails, but to a lesser degree The daughter has no palmar or plantar hyperkeratoses

All the nails are thickened, hard and brownish and present numerous close-set undulating striations On the heels and adjacent areas of the arch of the foot are multiple discrete pinhead-sized to split pea-sized horny papules There is a subacute dermatitis on both hands

DISCUSSION

DR SAUL S ROBINSON I wonder if the possibility of pustular psoriasis has been ruled out There is a suspicious lesion on one elbow that may fall into that group

DR C RUSSELL ANDERSON In this case of genodermatosis all the nails are involved The nails are thickened and discolored, present closely set undulating

transverse striations of the surface and lack the lunulas of normal nails. The symmetric hyperkeratosis of the soles complete the picture. A daughter who has the identical dystrophy of the nails lacks the plantar hyperkeratosis. However, I am sure this condition will occur eventually as it did in her mother.

Dermatitis Herpetiformis Perstans Presented by DR. MAX J. WOLFF and DR. JOHN D. ROGERS (by invitation)

E. M., a man aged 32, presents an eruption on the shoulders of three years' duration. The eruption appeared for the first time three years ago in the form of a blister on the right shoulder. Small blisters soon appeared about this initial lesion. An ulceration appeared in this area the size of a half-dollar and persisted for three and one-half months before healing with treatment. In the meantime vesicular areas appeared on the back which did not heal. There are no subjective symptoms. During the past five months the patient has not been free from lesions at any time.

The dermatologic examination reveals a herpetiform eruption on the shoulders, with an advancing margin. Some bullous lesions are also present. There is some atrophy at the site of healed lesions. Slight erythema is present about the vesicular and bullous lesions.

The feces and urine were normal. The Wassermann reaction of the blood was negative.

The therapy consisted of the local application of one-fourth erythema doses of roentgen rays (75 r), ultraviolet radiation, aniline dye and an ointment containing chlormercuryphe nol. The patient was also given a series of eight smallpox vaccinations. There has been no improvement from any therapy.

DISCUSSION

DR. NELSON PAUL ANDERSON: I believe that the condition in this case is dermatitis herpetiformis repens recurrens. In Atlanta the condition would be called familial benign pemphigus (Hailey), while in Baltimore it would be termed Darier's disease with bullous lesions. The fact remains that this is one and the same clinical entity. I think that a review of these articles will show that they deal with the same disease. Strangely enough, this patient is unable to recall any members of his family who have this disease. I should like to see another microscopic section from one of the lesions on the right shoulder. For treatment, I recommend a few therapeutic doses of sulfanilamide.

DR. WILLIAM H. GOECKERMAN: I have nothing to add. To me this case seems to be the most interesting one of the evening. If Dr. Anderson's discussion is correct, the condition is a new entity that I could not put a label on. It is not an ordinary herpes.

DR. SAMUEL AYRES, JR.: This case corresponds to the group of 5 cases I reported as herpetiform dermatitis repens. The eruptions often begin with lesions which resemble herpes simplex. They heal centrally and then slowly spread peripherally like dermatitis repens. I had my first case the first year I came to Los Angeles, nineteen years ago. I have since had 5 cases that were identical. In all there were lesions around the neck. I should like to hear about any additional ones. I have not been able to find any permanent cure. All the patients would respond to a few fractional doses of roentgen rays, but the condition would come back again. I think that it is the same picture Pels and Goodman described (ARCH. DERMAT. & SYPH. 39:438 [March] 1939) and the same one which the Haileys (ARCH. DERMAT. & SYPH. 39:679 [April] 1939) described recently under the name chronic benign familial pemphigus. Which designation is better I do not know. The designation herpetiform dermatitis repens is purely descriptive, suggesting a resemblance to herpes simplex and to dermatitis repens. The name was not intended to suggest an etiologic relation to either condition or to dermatitis herpetiformis.

DR KENDAL FROST I have a patient with lesions of this type who has been regularly under my observation for about eighteen years. After observing him for some years, I finally made a diagnosis of pemphigus of the Senear-Usher type. The lesions in the patient presented today were identical with a phase through which the lesions pass in my patient. I also believe that the cases which Dr Ayres has been describing belong in this group.

DR H SUTHERLAND CAMPBELL I feel that the case should fall in the first mentioned category.

DR SAUL S ROBINSON I have at present under my care a brother and sister with this disorder, which has been recurrent four to five years. In this instance the sister has only been seen one and one-half to two years. I had success with calcium gluconate injected intravenously. Often roentgen rays and local applications failed to heal the disease.

DR MAX J WOLFF I saw the patient for the first time this evening. I was impressed by the fact that some of the patches suggested atrophy.

Multiple Benign Epitheliomatosis Presented by DR MAX J WOLFF and DR JOHN D ROGERS (by invitation)

E S, a retired druggist aged 72, presents a scar in the left gluteal region at the site of removal of a fungating mass. Scaling oval lesions have been present on the chest, back and abdomen for two and one-half years and have recently spread to the gluteal and inguinal regions.

The lesions on the trunk are multiple oval brownish red macular plaques. The histologic examination of tissue removed from the fungating mass showed basal cell epithelioma.

DISCUSSION

DR NELSON PAUL ANDERSON I believe that this eruption is due to arsenic. He has one arsenical keratosis on the flexor aspect of the right index finger. He is a druggist, and he probably has taken arsenic during his lifetime, although he states that he has not.

DR H SUTHERLAND CAMPBELL I agree with the diagnosis.

DR KENDAL FROST I thought I could see tiny punctate keratoses along the side of the palm.

DR WILLIAM H GOECKERMAN I would rather call the lesions superficial than benign, because some of them, while they last for years, eventually become prickly cell carcinomas.

Lupus Erythematosus Presented by DR WILLIAM H GOECKERMAN

L I H, a man aged 42, presents a slowly spreading lesion on the scalp of several years' duration. There are old scarred areas of lupus erythematosus on the face that have been treated with radium. The physical examination reveals arsenical keratoses on the palms and fingers. On the frontal region of the scalp is a palm-sized area showing characteristics of lupus erythematosus.

The case was presented for therapeutic suggestions. The lesions on the scalp present an individual problem. The patient has had radium therapy for facial lesions, with satisfactory results, and believes that he should have the benefit of such treatments for the scalp also. He has had injections of bismuth compounds and gold compounds, applications of solid carbon dioxide and removal of foci of infection.

DISCUSSION

DR H SUTHERLAND CAMPBELL This patient came to see me some three or four months ago. At that time he appeared to be under great nervous stress. He gave a somewhat rambling history of having been treated for several years by different dermatologists and stated that he had received many injections of a

gold compound. He concluded by stating that now "they want to x-ray my head" I informed him that the best thing for him to do was to go away and forget about the condition for a while, as a rest from therapy might benefit him. He returned some three weeks later much tranquilized, he was given some ichthammol salve and told to use it for a few weeks. He returned a fortnight later, and I was much surprised at the local benefit, whether from the rest period, the ichthammol or his own economy. I did not see him after that until tonight.

DR SAMUEL AYRLS JR. I presume the question of focal infection has been taken care of. How long is it since he has had gold therapy? I should be inclined to give him another course of gold treatments. Sometimes when a person does not respond at one time he may do so at another time.

DR KENDAL FROST. I saw this man in 1937. He had been treated with solid carbon dioxide and radium but not with gold compounds. He wanted treatment with plastic surgical procedures, which had been used on some lesions on the face without their recurrence. I advised him to have gold therapy, as he had never had that, and gave him twenty injections of a gold compound, the last five being of 100 mg each. He did not improve and may have even become a little worse. The step I wanted to take was to combine gold and solid carbon dioxide, but he refused. I gave sulfanilamide or azosulfamide (neoprontosil, disodium 4-sulfamidophenyl-2'-azo-7'-acetylamino-1'-hydroxynaphthalene-3',6'-disulfonate) to a group of patients with chronic discoid lupus erythematosus at the Los Angeles County Hospital last spring, without any change in the condition, and decided that the drugs were worthless in this disease.

DR C. RUSSELL ANDERSON. The use of sulfanilamide in the treatment of lupus erythematosus proved disappointing to me. I had 1 patient with subacute disseminated lupus erythematosus in which dissemination occurred after two days' use of azosulfamide (neoprontosil). Recently varicella developed in a patient of mine who had chronic discoid lupus erythematosus which had proved resistant to all treatment. Ten days later there had occurred a good 90 per cent clearing of all the lesions. This suggests the use of nonspecific measures, such as foreign protein therapy. Some time ago Dr Samuel Becker of Chicago told me of a patient of his who had chronic discoid lupus erythematosus which was resistant to all treatment and in whom the use of potassium iodide produced clearing of the lesions.

DR H. SUTHERLAND CAMPBELL. I think that these observations are common in regard to lupus erythematosus. I have had 4 or 5 cases in which adequate gold therapy had been given, with little to no result. In each case the condition cleared up rather spectacularly after therapy with iodobismutol.

DR ARTHUR FLETCHER HALL JR. A strict salt-free diet might be combined with whichever form of treatment may be decided on. I have had 2 patients who responded at first to gold therapy and later showed no further response until they were given a salt-free diet, when they improved tremendously, only to relapse when the diet was ignored. Gold sodium thiosulfate was continued along with the diet.

DR HARRY P. JACOBSON. I subscribe to the diagnosis of lupus erythematosus, as presented. It is agreed more or less, of course, that this clinical entity probably represents a cutaneous reaction to a focus of infection of one kind or another. The successful therapeutic management of these cases usually depends on the enhancement of the immunity mechanism of the patient by medicaments and therapeutic agents of various sorts. In some cases injections of a gold compound answer the purpose. At other times a bismuth compound serves just as well. Then again, neither of them seems to influence the condition. I have observed an occasional case in which the condition responds fairly satisfactorily to non-specific protein medication in the form of defatted boiled milk injected intramuscularly. I believe that it would be worth while to try this method of treatment in this particular case.

CHICAGO DERMATOLOGICAL SOCIETY

EDWARD A. OLIVER, M.D., *President*HERBERT RATTNER, M.D., *Secretary*

Oct 18, 1939

Lupus Erythematosus (Extensive) Presented by DR FRANCIS E. SENEAR and DR EARLE R. PACF (by invitation)

M. C., an Italian woman aged 50, was sent to the dispensary of the Research and Educational Hospital, University of Illinois, on Oct 2, 1939, with an eruption of about four months' duration. It involves the arms, the upper part of the chest and shoulders, the neck and the areas about the ears and temples, and consists of small papules to coin-sized patches, often confluent, and on the temporal scalp reaching the size of half a palm. They have a striking violaceous color, and many papules and annular groups strongly resemble those of lichen planus. Follicular accentuation is notable in the scalp lesions, and on the interseapular area it reaches the proportions of lichen spinulosus. On the sides of the neck particularly the skin is thickened, becoming almost vegetative in places. There is little or no loss of hair in the scalp lesions (present about six weeks) and no visible atrophy. There are no lesions on the mucous membranes of the mouth. The patient has lost 12 pounds (5.4 Kg) and has unusually severe headaches. Pruritus is moderate.

The Wassermann and Kahn reactions were negative. The white blood cell count was 6,100 per cubic millimeter, with normal differential values. Histologic examination of a well developed lesion on the neck was reported by Dr M. R. Caro.

There was a thin scale. The epidermis was thinned over the infiltrated areas and slight edema showed, especially in the basal cells. In the upper part of the corium there were many nests of densely packed cellular infiltration that formed nearly a continuous layer. These were composed largely of lymphocytes. About a hair follicle and about the superficial blood vessels there were mantles of the same cellular infiltration.

DISCUSSION

DR LOUIS A. BRUNSTING, Rochester, Minn. It is my opinion that this condition is lichen planus, from the clinical and microscopic standpoint. Lupus erythematosus to this extent would ordinarily be associated with a much more systemic reaction.

DR M. E. OBERMAYER. Clinically the condition resembles lupus erythematosus. The loss of hair and the distribution of the lesions are in favor of that diagnosis. Looking over the slide, however, I found the histologic picture to be hardly compatible with lupus erythematosus but rather typical for lichen planus. I agree with Dr Brunsting as to the latter diagnosis.

DR OLIVER S. ORMSBY. While there may be some question in diagnosis between subacute lupus erythematosus disseminatus and lichen planus, I do not believe that the absence of constitutional symptoms would rule out lupus erythematosus. I have seen a number of patients with the subacute variety, with no constitutional symptoms, who had as extensive an eruption as is present here. The condition will probably prove to be subacute disseminated lupus erythematosus rather than lichen planus.

DR S. W. BECKER. There was some thinning of the epidermis in the sections, which I do not believe would be present in lichen planus. A point which was not emphasized and which is important is the spinous nature of the lesions. In patients of this type in whom gold dermatitis develops the dermatitis would be of the lichen spinulosus type. I also believe that this condition is lupus erythematosus.

DR MAURICE OPPENHEIM (by invitation) I consider the condition to be lichen planus. The atrophic areas are bluish, whereas lesions of lupus erythematosus should be reddish. The histologic observations of hyperkeratoses, round cell infiltrations, certain changes in the blood vessels and the presence of a space between the infiltrate and the cutis, which is never seen in lupus erythematosus, indicate the diagnosis of lichen planus.

DR M. R. CARO About six years ago (ARCH DERMAT & SYPH 29:477 [March] 1934) I presented before this society a case almost identical with this as a case of lichen planus. The histologic picture was also similar. At that time Dr Finnerud made the statement that when the condition resembles both lupus erythematosus and lichen planus it is usually lupus erythematosus. My patient's course at that time showed that statement to be true. I think that in the present case the histologic picture is consistent with the diagnosis of lupus erythematosus.

DR HERBERT RATTNER During the time that it was my duty to watch the society transactions carefully, there were 4 or 5 cases reported in which the diagnosis was either lichen planus or lupus erythematosus. As I recall, in each instance the final diagnosis was lupus erythematosus.

DR FRANCIS E. SINEAR Last month Dr Wile showed me a patient at Ann Arbor with a condition similar to the one presented today. In his patient too the lesions were notably spiny and had the clinical appearance of lichen planus pilaris in that the lesions were grouped. That patient had definite lichen planus lesions in the mucous membrane and a typical histologic picture of lichen planus. When I saw the present patient about two weeks ago I was struck immediately by the resemblance and felt that the condition was probably lichen planus. I do not think the color can be used as a differentiating point in this case. The patient is of Italian origin and has a distinctly dark skin. I think that lupus erythematosus is frequently seen in dark-skinned patients with changes in color similar to those in lichen planus. While it is known that lichen planus occurs on the face, I feel that the condition in this patient will prove to be lupus erythematosus, in spite of my original opinion to the contrary.

A Case for Diagnosis (Atypical Psoriasis?) Presented by DR DAVID V. OMENS

G. F., an American housewife aged 39, presents on both hands and feet a sharply defined patchy erythematous condition of the skin, with involvement of all the nails, of three and one-half years' duration. The skin is infiltrated and somewhat atrophic and presents scaling. The patient has been married for fifteen years, she has two children, aged 14 and 10 years, respectively, her third pregnancy terminated in a miscarriage at five months. Her husband is living and well; the family history is not significant. Serologic tests of the blood gave negative results. The patient would not grant permission for a biopsy.

DISCUSSION

DR E. P. ZEISLER I think that the diagnosis should rest between pityriasis rubra pilaris and a symmetric keratoderma.

DR M. E. OBLERMAIER This condition is a psoriasiform eruption, and I cannot understand how ordinary psoriasis can be ruled out without a biopsy. Clinically the diagnosis rests between psoriasis and pityriasis rubra pilaris.

DR OTTO H. FOERSTER, Milwaukee I believe that psoriasis should be considered first and pityriasis rubra pilaris second.

DR M. J. REUTER, Milwaukee This woman has atrophy and whitish striae on the tongue, which brings up the question of so-called submucous thrush. In addition, there is slight involvement of the angles of the mouth.

The entire picture could possibly be explained on the basis of moniliasis, and it might be well to have cultural studies made.

DR MAURICE OPPENHEIM (by invitation) The diagnosis in this case seems to me to be a tinea infection, because the margins of the lesion are round and the scales are attached at the periphery and raised from the central base

DR LOUIS A BRUNSTING, Rochester, Minn The diffuse smooth keratoderma of the palms and soles is not related to a fungous infection, although the condition of the nails and the involvement of the skin might be interpreted in that way I agree that the condition is perhaps atypical psoriasis There is smooth atrophy of the tongue, which is probably distinct from the dermatologic condition, and it may be well to study the gastric secretions for absence of hydrochloric acid and the blood for evidence of pernicious anemia Mention has been made of submucous thrush It is my experience that conditions thought to be thrush usually prove to be lichen planus or lupus erythematosus, if the cases are observed over a sufficiently long time

Arsenical Pigmentation and Keratoses First Manifested in Patient at the Age of Six Years Presented by DR J R WEBSTER (by invitation) and DR W W TOBIN (by invitation)

A F, aged 8½ years, is presented from the outpatient department of Children's Memorial Hospital

At birth there was cerebral hemorrhage necessitating spinal puncture which cleared the immediate symptoms, but the child has since had some choreiform and epileptiform symptoms Four and one-half years ago a physician gave him solution of potassium arsenite, 3 drops four times a day for a while, but later the dose was taken once a day He continued to take this dose for two years At the end of this period a more or less generalized dermatitis developed When this condition subsided the patient's family became aware that there was a change in the color of his skin It is not clear from the history as to when the skin of the hands and feet became rough He has taken no more solution of potassium arsenite since that time

The texture of the skin as a whole is rather harsh and dry, and on the covered portions of the body and extremities, especially noticeable about the axillas, there is a mottled, grayish brown pigmentation In addition to this there are moderate diffuse keratotic scaling of the palms and soles and sides of the feet and small localized punctate keratoses

The Wassermann reaction of the blood was negative Scrapings from the feet failed to show the presence of fungi either in potassium hydroxide preparations or in culture A Reinsch test performed on hair clippings last month (two years after discontinuance of arsenic medication) gave negative results for arsenic

DISCUSSION

DR FRANCIS E SENEAR I cannot recall ever having seen arsenical dermatitis in a child of this age

DR EDWARD A OLIVER Years ago I saw a boy in the Children's Memorial Hospital who had been taking 1 Gm (15 grains) of arsenic a day for five years Plantar and palmar keratoses developed

DR W W TOBIN (by invitation) We showed this patient largely for suggestions as to treatment We intend to try *agerite alba* in a patch test on some covered portion of the body to determine whether depigmentation will occur

DR EDWARD A OLIVER I think that it is unusual for children to show such a reaction to arsenic, because they generally tolerate it

DR OLIVER S ORMSBY I believe that sodium thiosulfate might help, in adults it has been of service in my experience

A Case for Diagnosis (Neurodermatitis Gigantea?) Presented by DR MAX S WIEN and DR A H SLEPYAN (by invitation)

Miss G W, aged 25, states that for the past year she has had a quadrilateral patch of thickening of the skin on the left side of the neck and that the patch is gradually getting wider and thicker. There are no subjective sensations.

Histologic slides prepared under the direction of Dr M R Caro and slides examined by both Dr Caro and Dr Slepian revealed the following picture: the epidermis as a whole was irregularly acanthotic. There was an occasional zone of parakeratosis, while the granular layer for the most part appeared normal. In the upper rete there was considerable vacuolation of the rete cells, with intracellular edema. In the cutis the small capillaries were dilated, and there was a perivascular infiltration of round cells. Numerous chromatophores were scattered through the papillary zone. The elastic and collagen fibers appeared normal.

DISCUSSION

DR M R CARO: I thought that histologically the lesion was a lichenification.

DR MAX S WIEN: When we first saw this patient we suspected the possibility of Uina's cardlike scleroderma, but the histologic section did not confirm this diagnosis. A localized patch of amyloidosis was also considered. In view of a report by J Merenlander I suggested this diagnosis, and I am happy to have it confirmed by the discussers and by the histologic section.

Bullous Lupus Erythematosus. Presented by DR DAVID V OMLIN

D M, an unmarried Bulgarian aged 67, presents on the face, neck and scalp a mildly inflammatory, sharply defined process, with atrophy of the involved areas and discrete bullae situated on these areas. The condition is of eight months' duration.

Tuberculosis Verrucosa Cutis Presented by DR S W BICKER and DR M E OBERMAYER

F D, a man aged 47, was in the clinic on June 8, 1939. He presented an eruption on the left thumb which had started four years before as a paronychia with pus formation. The latter condition healed, and the present lesion spread from that area and has remained ever since. There are no subjective symptoms, but he "picks on it" to a certain extent. There is moderate to considerable improvement in the summer, but the condition has never been completely absent. Two years ago two injections of arsphenamine were given, without any effect on the lesions, and one year ago he had several treatments with roentgen rays, which failed to influence the eruption. Blood tests on several occasions have all given negative reactions.

Examination revealed nothing abnormal except the lesions on the left thumb and a compensated mitral insufficiency. On the palmar surface of the thumb are several verrucous plaques, about 0.5 to 0.75 cm in diameter, noninflammatory and slightly elevated. On the dorsal surface of the thumb are several nodules with elevated erythema, varying from 0.5 to 0.75 cm in diameter and elevated 3 mm.

The Wassermann and Kahn reactions were negative, and the urine was normal. Biopsies were performed on June 8 and July 24, 1939.

DISCUSSION

DR OLIVER S ORMSBY: I think that the diagnosis of tuberculosis verrucosa cutis can be successfully defended in this case.

DR MAURICE OPPENHEIM (by invitation): There is no doubt that the condition is tuberculosis verrucosa cutis. It is to be regarded as an occupational disease. It has been observed in laundry workers, butchers, furriers and persons employed in hospitals. It is usually due to the human type of tubercle bacillus, but sometimes the bovine type or the avian type is responsible.

DR S W BECKER The progress of this man's condition, we thought, was rather unusual because the original lesions either have healed or are healing. Instead of the condition spreading as a single nodular plaque, as it often does in tuberculosis verrucosa cutis, several more or less isolated lesions have developed over four and a half years. The first sections did not show any specific infiltrate at all but demonstrated a nonspecific infiltrate with numerous keratotic plugs. On cutting more sections we finally found tuberculoid tissue, and although we have not been able to demonstrate tubercle bacilli I think the condition is tuberculosis verrucosa cutis.

A Case for Diagnosis (Reticuloendotheliosis?) Presented by DR HERBERT RATTNER and DR TIBOR BLNDRK (by invitation)

D Z, a white woman aged 22, is presented from the Mandel Clinic of Michael Reese Hospital. On May 2, 1939, she was surgically treated for acute suppurative appendicitis. A month after the operation she noticed a papule in the left axillary line about 3 inches (7.5 cm) below the axillary pit. About four similar lesions appeared two to three weeks later in the left clavicular region, and during the following weeks many similar lesions appeared in both axillary pits, along the right axillary line, on the back and in the left inguinal and genitocrural regions.

Examination shows about thirty-five lesions from the size of a millet grain to that of a small bean. They are round and oval, papular and nodular, yellowish red to brownish red, of the consistency of a soft fibroma and arranged almost symmetrically. No itching or burning sensation is present.

The chemical examination of the blood showed sugar, 98 mg, nonprotein nitrogen, 34 mg, cholesterol, 204 mg, and total lipoids, 828 mg, per hundred cubic centimeters. She had an icterus index of 8.

Histologic examination was done by Dr Caro. There was a small circumscribed papule slightly elevated above the surrounding skin. The epidermis was thin and flattened, and beneath it was a densely packed cellular infiltrate which was well demarcated from the rest of the corium below. The infiltrated area was vascular and contained many large pale cells which formed densely packed strands and masses, between which were scattered collagen fibers. Just beneath the epidermis there were also many lymphocytes and connective tissue cells. Mantles of cellular infiltration of the same type extended more deeply about the blood vessels. Staining with sudan III showed that many of the large cells that resembled ganglion cells contained lipid droplets in the cytoplasm. Elastic fibers were absent from the infiltrated area.

DISCUSSION

DR E P ZEISLER The condition resembles closely the one reported by Dr O'Leary as ganglioneuroma. The diagnosis would have to be verified by histologic examination.

DR FRANCIS E SENEAR I agree with Dr Zeisler that this condition has a close clinical resemblance to that in the case reported by Dr O'Leary. I know that Dr Pusey saw the patient before Dr O'Leary did, and I saw her about the same time. It had been suggested that the condition might be nevoxanthoendothelioma, but it had no resemblance to the nevoxanthoendotheliomas that I had seen. It showed a resemblance, however, to the photograph of the lesion in the case reported by Jacoby and Grund (Jacoby, R, and Grund, J L. Endothelioma Cutis, *New England J Med* 202:1247 [June 26] 1930). The condition was reported by Dr O'Leary as a neuroganglioma, while other pathologists thought it was a reticuloendothelioma.

DR LOUIS A BRUNSTING, Rochester, Minn. What was the size of the lesion that was removed for examination?

DR M H EBERT I should like to ask Dr Brunsting if the reticuloendothelial cells of the neuroma in Dr O'Leary's case looked like those in the present case.

DR TIBOR BENEDEK (by invitation) The biopsy was made just a week ago and was of an early lesion

DR LOUIS A BRUNSTING, Rochester, Minn I think that the condition in this case is xanthoma in an early stage, which would explain the atypical microscopic picture The elevation of the lipids in the blood adds weight to this assumption

DR HERBERT RATTNER When I first saw the patient last week I was also impressed by the similarity of the condition to the one that Dr O'Leary reported as multiple ganglioneuroma of the skin His patient too was Jewish and of about the same age, both patients had had an appendectomy preceding the outbreak of the eruption Our patient has fewer lesions, but the morphologic characteristics are the same discrete yellowish soft papules and nodules, symmetrically placed on the trunk The blood lipids were elevated in both cases Dr O'Leary's patient had also consulted Dr Pusey, and it was in Dr Pusey's office that I first saw him The clinical picture that he presented, which first suggested xanthoma tuberosum, was unusual, and the microscopic picture was interpreted by the late Dr Jaffé as cutaneous reticuloendotheliosis Later the patient appeared at the Mayo Clinic, and a diagnosis was made of multiple ganglioneuroma, because of the presence in the sections of Nissl granules and dendritic processes It is my impression, however, that Dr Jaffé did not agree with this interpretation of the microscopic picture and that various other pathologists in the country could come to no agreement In general, the neuropathologists stated the belief that the condition was ganglioneuroma, and the general pathologists, that it was reticuloendotheliosis

Our first slides show the presence of numerous histiocytes, those stained for nerve tissue have not yet been completed We presented the patient today because we feared there would not be another opportunity to do so

NOTE—Special stains failed to show nerve tissue

DR M R CARO I saw the slides which Dr Jaffé examined a number of years ago I was struck by the resemblance of the cells in the present sections to those in the other case I suggest that another biopsy be performed twenty-four hours after injecting a few drops of a 10 per cent solution of saccharated ferric oxide into a lesion If these cells are from the reticuloendothelial system they will take up the iron

DR S W BECKER I should like to give a word of warning about the use of saccharated iron oxide If over a 1 per cent solution is used, it enters the cells by diffusion A 1 per cent solution is taken up only by phagocytic action

A Case for Diagnosis (Basal Cell Epithelioma of Glans Penis?) Presented by DR J H MITCHELL

E S, aged 61, was first seen on Feb 29, 1936, with a lesion which had begun as a small papule at the meatus of the glans penis and which had gradually extended for the past seven years The patient had been treated for doubtful syphilis twenty-eight years prior to the onset, but there had been no treatment for the lesion on the glans There had been a continuous mild urethritis for years, but there was nothing in the history suggesting gonorrhea The Wassermann and Kahn reactions were negative both before and after a series of injections of neoarsphenamine, which had little if any influence on the lesion Later 350 r of ultraviolet rays from a quartz mercury vapor glow lamp ("cold quartz lamp") was administered, with decided benefit The patient was presented at the meeting of the Chicago Dermatological Society in May, but the published proceedings included only 8 of the cases presented at that meeting, and this case was omitted A biopsy was not obtained at that time

The patient was not seen again until Oct 18, 1939 The lesion gradually extended until it involved about twice as much area as when first seen The

appearance, however, remains the same, and the urethral discharge has continued. There are a few insignificant inguinal glands. There is tenderness, and manipulation leads to bleeding. The Wassermann and Kahn reactions are negative.

The meatus is surrounded by a well defined, bright red, slightly elevated, somewhat verrucous lesion, after retracting a long prepuce. Tissue for biopsy was removed by means of the cutting loop.

Histologic examination gave the following results. The rete pegs were much elongated and widened. Basal cell epithelioma was suggested, but the diagnosis is not definite. No evidence of Bowen's disease or Paget's disease could be found. Clinical photographs of the lesion as it appeared in 1936 and in 1939 are presented.

DISCUSSION

DR MAX S WIEN. During my service at Cook County Hospital there were 2 cases of a similar condition which was diagnosed as erythroplasia of Queyrat, and the diagnosis was confirmed by the histologic study made by Dr Jaffé. After my experience with these 2 cases in my opinion such conditions should be looked on as potentially highly malignant cancer and treated as such. While the patient is under observation a transition may occur rapidly from a simple type of basal cell cancer to highly malignant prickle cell cancer. These conditions are resistant to radiation, and for that reason the best treatment seems to be some destructive method, such as electrodesiccation. The lesion starts as a smooth red velvety elevated patch that may break down to a moist fungating lesion, with partial destruction of the corona. When this stage is reached therapeutic measures must be drastic, and I should advise early amputation with a careful "cleaning out" of any involved inguinal glands. Recently at a meeting of the Cleveland Dermatological Society (*ARCH DERMAT & SYPH* 40 456 [Sept] 1939) LaRocco presented a patient with this condition, and in the discussion the members stated the opinion that some form of excision or amputation was indicated.

DR LEONARD F WRBET. I should like to ask Dr Mitchell how long the lesion has been present.

DR J H MITCHELL. The lesion has been present for ten years. In three years it has grown slowly.

DR M J REUTER, Milwaukee. I thought there was some suggestion in the slide of a basal-squamous cell epithelioma.

DR S W BECKER. I should hate to base an opinion on one section, but either the rete processes were cut on the bias or there was some penetration of the epithelial tissue into the cutis. I should be suspicious that the lesion is already malignant, but it is not the squamous variety of epithelioma which usually arises in this region.

Herpes Zoster in an Infant Three Months Old. Presented by DR THEODORE CORNBLEET

R R, an infant girl aged 3 months, presents an eruption on the lateral surface of the right hand and the lower part of the forearm which developed ten days ago. The lesions are small grouped vesicles which remain more or less intact. In the fold at the wrist some of the vesicles have broken down and formed an abraded area. The lesions came on suddenly. There is no evidence of scratching. The baby was not previously exposed to chickenpox or herpes.

Lymphatic Leukemia. Presented by DR M H EBFRT

J K, a Greek aged 60, whose occupation is that of a clerk in a fruit and vegetable store, began to be troubled with pruritus three years ago. An eruption gradually appeared on the hands, forearms and thighs, with an increase in the intensity of the pruritus and scaling and thickening of the skin, which have become progressively greater until the entire cutaneous surface is involved.

The skin of the entire body shows thickening, with fine branny scales, and bronzing. There is generalized adenopathy, the lymph nodes being freely movable and discrete. There have been three pyodermic flare-ups since his admission to the hospital in July.

The Kahn reaction was negative. Chemical examination of the urine and blood gave normal results: 67 per cent hemoglobin, 3,380,000 red blood cells and 56,400 white blood cells per cubic millimeter, with a differential count of 10 per cent lymphoblasts, 4 per cent monocytes, 42 per cent young lymphocytes and 44 per cent polymorphonuclear neutrophils. In the sternal puncture the particular portions of the bone marrow examined showed no unusual lymphoid invasion.

A roentgenogram of the chest showed no mediastinal abnormality.

Hodgkin's Disease. Presented by DR THEODOR CORNBILLT and DR HERBERT RATTNER

A P, a white man aged 44, gives a history of an eruption beginning about September 1939. He first noticed the eruption on the dorsal surfaces of the hands, from there it spread to the forearms and then became generalized. It was accompanied by severe pruritus. He works in a foundry and attributed his eruption to the excessive heat and perspiration.

Examination reveals erythema, scaling, fissuring and slight weeping of the skin of the face and neck. There is scaling of the dorsal surfaces of the hands and forearms. There are excoriated areas on the lower part of the abdomen and edema, induration and scaling on the legs. All accessible glandular areas, including the posterior cervical nodes (epitrochlear, axillary and inguinal), show bilateral enlargement.

The blood count showed 4,860,000 red cells and 10,000 white cells per cubic millimeter, with 66 per cent polymorphonuclear leukocytes, 10 per cent eosinophils, 14 per cent lymphocytes and 10 per cent monocytes. Chemical examination of the urine and blood gave normal results. The Kahn test gave a negative reaction. A roentgenogram of the chest was normal.

Histologic examination of the skin showed moderate acanthosis of the epidermis, with edema and infiltration of the papillary body by a large number of round cells. The picture was interpreted as a nonspecific one. Histologic examination of a lymph gland showed (1) polymorphism of cells, (2) reticulum cell hyperplasia, (3) eosinophilia and (4) Sternberg giant cells.

DISCUSSION

DR FRANCIS E. SANFAR: I think that the first case is interesting because the condition is an example clinically of Hebra's pityriasis rubra, which is sometimes due to a leukemic process. It reminds one of a case presented here (*ARCH DERMAT & SYPH* 13:551 [April] 1926) in which a diagnosis of pityriasis rubra of Hebra was accepted with no thought of the leukemic process. When the society visited Dr. Wile's clinic a year later (*ARCH DERMAT & SYPH* 18:483 [Sept] 1928) the same patient was there with a well developed blood picture of leukemia.

DR LEONARD F. WEBER: I saw the patient with Hodgkin's disease when the eruption was limited to the legs and forearms. At that time he had generalized adenopathy. The legs and forearms today show considerable improvement, but at the present time he has a definite involvement of the trunk and thighs. I understand that the improvement can be attributed to roentgen ray therapy given at the Cook County Hospital.

DR MAURICE OPPENHEIM (by invitation): The clinical features of pityriasis rubra Hebrae are universal erythroderma, infiltration of the entire skin, general glandular induration and later atrophy of the skin, with fatal ending. Jadassohn published many years ago an important paper in the *Archiv für Dermatologie und Syphilis* (Jadassohn, J. *Arch f Dermat u Syph* 23:941, 1891, *ibid* 24:85, 273).

and 463, 1892) in which he tried to find a connection between the pityriasis rubra of Hebra and tuberculosis. In a great number of cases the diagnosis of pityriasis rubra of Hebra is made without reason, because a similar condition is observed as a prestage of various cutaneous diseases, such as the prefungoid stage of mycosis fungoides and the prestage of lymphogranuloma (Hodgkin's disease) and leukemia. In Vienna I observed only 2 cases of real pityriasis rubra of Hebra. *Dermatitis atrophicans progressiva* (*atrophia cutis idiopathica*) resembles the description which Hebra made of his disease. Only the fatal end is absent. I think that the question as to whether pityriasis rubra of Hebra is a special type of cutaneous disease or whether it embraces different types which have only common features must be studied anew on the basis of modern knowledge of exfoliative erythroderma.

Koilonychia Presented by DR THEODORE CORNBLEET

F. G., a white woman aged 41, has had concavities of several finger nails for several years. She also has psoriasiform patches of chronic dermatitis on both knees. Similar patches were previously present on the elbow and on the back of the neck. Examination of the blood shows 3,100,000 red cells and 6,400 leukocytes per cubic millimeter and 64 per cent hemoglobin.

DISCUSSION

DR HERBERT RATTNER: I have seen the statement that the presence of koilonychia invariably indicates that the patient has microcytic anemia, but I have noticed spoon nails in a person who had psoriasis but not anemia.

DR THEODORE CORNBLEET: I have observed 1 other patient who had this condition and also microcytic anemia. The patient just presented improved definitely on therapy with liver and iron.

A Case for Diagnosis (Psoriasis?) Presented by DR M. H. EBERT

Mrs. E. H., aged 42, of German descent, was presented to the society in March 1939 (ARCH. DERMAT. & SYPH. 40:632 [Oct.] 1939) with a symmetric eruption on the neck, trunk and extremities of reddish patches covered with fine silvery scales and, in places, crusts. The lesions on the face were maculopapular, with small adherent scales and crusts, the lips were scaly, the tongue was somewhat smooth, and the gums were red but not spongy. On the legs the lesions did not fade with pressure. At that time there was a history of drinking 1½ gallons of beer daily for five or six years and of an inadequate diet. Blood ascorbic acid was 0 on admission to the hospital. She was discharged from the hospital as perfectly well seven weeks after admission but she failed to return to the dermatologic clinic.

Her present condition, she stated, began in July, about two months after she left the hospital, with redness, swelling and scaling of both thumbs. The condition gradually spread over the dorsa of the hands and the rest of the body, until when she reentered the hospital, on August 25, she presented the same picture as before except for the absence of hemorrhages on the legs. The patient's family stated that she has been drinking beer in preference to eating.

Laboratory Tests.—The urine was normal. The ascorbic acid content on October 4 was 0.8 mg. per hundred cubic centimeters, on October 11 it was 0.4 mg. per hundred cubic centimeters, and on October 18, 17.4 mg. per hundred cubic centimeters. A Kahn reaction was negative. The icteric index was 5.

A blood count showed 75 per cent hemoglobin and 4,150,000 red blood cells and 6,000 white cells per cubic millimeter, with a normal differential count. The ascorbic acid content of the blood on October 4 was 0.1 mg. per hundred cubic centimeters, on October 11 it was 0.3 mg. per hundred cubic centimeters, and on October 18, 8.5 mg. per hundred cubic centimeters.

Chemical examination of the blood showed 58 mg nonprotein nitrogen per hundred cubic centimeters, 4.83 per cent proten, 2.6 per cent albumin and 2.23 per cent globulin. The chloride content was normal. The sugar content of the blood on September 29 was 67 mg per hundred cubic centimeters. The fasting sugar content on October 18 was 50 mg per hundred cubic centimeters. The sodium and potassium values were normal.

DISCUSSION

DR E. P. ZEISLER: I thought that the condition might be an early stage of mycosis fungoides.

DR FREDERICK R. SCHMIDT: I thought that arsenic might be considered as a cause. In taverns the coils of the beer barrels are cleaned with a solution often containing arsenic. Many cases of conditions resembling psoriasis were reported in Germany in a group of soldiers who drank beer containing arsenic.

DR DAVID V. OMENS: It is a common practice among tavern owners to have the beer coils washed with an arsenical solution. Sometimes the first person to get beer after the washing gets a dose of the arsenic.

DR MAURICE OPPENHEIM (by invitation): I thought that the condition was an arsenical dermatitis. One can determine whether it is or not by making skin tests. Different preparations of arsenic (trivalent, pentavalent, inorganic and organic) give different results and are specific, as in other cases of hypersensitization. In Vienna cases of arsenic intoxication were often observed in which the condition was due to wall dye and wall paper. It is not only the green color that causes intoxications. Up to the present, no one knows in which way the arsenic enters the organism. In every suspicious case examinations are made of the hair, nails, scales and urine. Observations of arsenic in the skin are manifold. Sometimes arsenic is found in the hairs of the scalp and sometimes in the hairs of the axillae; yet a diagnosis of arsenic intoxication is made only when arsenic has been found in the wall dye or wall paper and in the organism.

DR THEODORE CORNBLFET: There was some question about a deficiency of vitamin C producing this eruption. It is well known that various infections and intoxications may deplete the source of vitamin C in the body. In several patients with diffuse dermatoses I observed the same result. I think, however, that one would have to have more grounds before attributing the dermatosis in this case to a deficiency of vitamin C.

DR LEONARD F. WEBER: Dr Oppenheim mentioned last month at the meeting the chance of arsenic being in wall paper. Several manufacturers of wall paper in Chicago and Joliet maintain that arsenic is not used in its manufacture.

DR HERBERT RATTNER: I think it should be stated that when this patient was presented in March the possibility of arsenical dermatitis was suggested. The nails, hairs and scales were examined for arsenic, but with negative results, and histologic studies failed to substantiate a diagnosis of psoriasis or mycosis fungoides.

DR MAX WIEN: The last time this patient was presented her condition was believed to be scurvy. I think she should be treated with vitamin K and bile salts. This combination has been successful in certain cases of blood dyscrasia associated with avitaminosis.

Hemolymphangioma (Preponderant Hemangioma Transformed to Lymphangioma) Presented by DR THEODORE CORNBLFET

Reddish and clear translucent excrescences are present on the left arm and adjacent thorax of this patient. On several occasions a phlebitis has developed, with fever and symptoms of toxicity. The lesions have changed from a preponderance of the hemangioma element to an increased amount of the lymphangioma portion. After each phlebotic attack this transition has become accentuated.

DISCUSSION

DR WALTER W TOBIN (by invitation) I have observed this patient for about two years. When I first saw her she presented about the same picture as now, perhaps somewhat worse. She was treated with solid carbon dioxide, and tremendous edema of the chest wall developed, with no constitutional symptoms. After this subsided fractional doses of roentgen rays were given. There was some improvement. Her condition is 50 per cent better today than when I treated her two years ago. There are perhaps more lymphangiomatous lesions and fewer hemangiomatous lesions. The deep doughy involvement about the elbow is unchanged.

DR THEODORE CORNBLEET Considering the preponderance of hemangion elements, I thought that the condition might be given the title *hemolymphangioma*.

A Case for Diagnosis (*Erythema Multiforme?* Drug Eruption?)

Presented by DR THEODORE CORNBLEET and DR HERBERT RATTNER

Mrs. A. S., aged 49, noticed pruritic vesicles on the trunk and extremities about one year ago and went to a Chicago hospital, where a diagnosis of pemphigus was made. After discharge she remained well until September of this year, when blebs which itched developed on the lower extremities and also an intertrigo of the breasts. She remained in the Cook County Hospital for two and a half weeks and was discharged as perfectly well. The day after leaving the hospital she again had pruritus of the legs, with the formation of bullae and pinpoint-sized red areas on the thighs. The only medication she has been taking is cascara for constipation and acetylsalicylic acid, 2 tablets three or four times a day two or three times a week for headache. About two weeks ago a sore throat developed, for which she took a liquid medicine and some powders prescribed by a physician.

Examination shows nondescript erythematous scaly patches on the right cheek, intertrigo of the breasts, nonblanching pinpoint-sized red areas on the thighs and circumscribed round denuded areas with erythematous haloes and bullae with erythematous borders on the legs. The throat is red, and the anterior cervical glands are enlarged, especially on the right side.

Laboratory Tests—A smear of bullous fluid revealed many polymorphonuclear leukocytes. The urine was normal. A test for bromides and iodides gave negative results. Examination of the blood showed 80 per cent hemoglobin and 7,200 white cells per cubic centimeter, with a differential count of 76 per cent polymorphonuclear leukocytes, 4 per cent eosinophils, 14 per cent lymphocytes and 6 per cent monocytes. The red blood cells numbered 4,800,000 per cubic millimeter. The fasting blood sugar was 88 mg per hundred cubic centimeters, and the Kahn reaction was negative.

DISCUSSION

DR OLIVER S. ORVISBY I think that this condition is a toxic eruption. Whether the toxemia comes from a drug or from other sources makes little difference. I should not class it as *erythema multiforme*. On the extremities the lesions are purpuric. Purpuric lesions are seen not infrequently on the lower extremities, with erythematous lesions elsewhere. The condition has all the manifestations of a toxic eruption.

DR FRANCIS E. SENEAR I agree that the follicular location of the lesions would rule out *erythema multiforme*, and I believe that the eruption is a toxic manifestation.

DR HERBERT RATTNER This visit to the hospital is the patient's second. The first time the lesions were fungating she had been taking drops, and it was assumed that the eruption was due to halogens. Today, however, the eruption is more that of *erythema multiforme*.

Lichen Planus Presented by DR DAVID V OMENS and DR WALTER W TOBIN (by invitation)

J K, a woman aged 45, states that six weeks ago itchy red spots appeared on her arms, and within a few days they appeared all over her body with the exception of the area covered by a bathing suit and her palms. She had been exposed considerably to the sun while wearing a bathing suit. She has been under unusual nervous strain because of a death in the family and economic difficulties.

Prior to admittance to the hospital she had received four intramuscular injections each of 0.13 Gm of bismuth subsalicylate at weekly intervals. Four days ago, because of swelling of the lower part of her legs and the occurrence of a few large blisters on her legs and forearms, she entered the hospital.

She presents a generalized bluish erythematous papular and papulovesicular dermatitis, which is sharply margined where her bathing suit covered her. However, there are a few scattered flat-topped violaceous papules in the bathing suit area. The lesions on the legs and feet are larger and more hypertrophic. The face is somewhat involved, with the lips covered with dry adherent scales, and the buccal membranes show irregular whitish patches.

The Kahn reaction of the blood was negative. The blood count was normal, the results of examination of the urine were normal, and the blood sugar was within normal limits. Dr Gant stated that the patient's urine was too light in color to test for porphyrin.

DISCUSSION

DR LOUIS A BRUNSTING, Rochester, Minn. There are two features of unusual interest: the bullous character of the lesions on the hands and the involvement particularly in the regions exposed to the sun. I have seen this type of reaction in other cases of lichen planus, in cases of disseminated lupus erythematosus, in 1 case in which psoriasis followed roentgen therapy and also in a case in which lichen planus followed exposure to ultraviolet irradiation.

DR THEODORE CORNBLEET. Recently it has been reported that some persons sensitive to light may benefit from administration of an estrogenic substance.

DR OTTO H FORSTLER, Milwaukee. In patients with lichen planus who have been treated with roentgen rays directed to the spinal sympathetic areas, especially in those with generalized eruptions and more often in women, it is not unusual to have a dense eruption of spinulous lesions of lichen planus develop in the irradiated area, in some instances with a few scattered discrete spinulous lesions at a distance, as on the shoulders or hips.

DR LEONARD F WEBER. I have been impressed several times with the direct benefit derived from sunlight in patients with lichen planus. This observation has been noticed more than once in patients who take a winter vacation in Florida. In this case the condition is the direct opposite: the lichen planus is worse after exposure to sunlight.

DR S W BECKFR. In regard to the effect of sunlight, it is known that moderate exposure to sunlight, especially in Florida, will always benefit lichen planus. The same applies to psoriasis. But if a psoriatic patient is overexposed, there occurs a shower of lesions in the sites sunburned by ultraviolet rays.

DR DAVID V OMENS. This patient could be closely followed, we have had her under observation for six or eight weeks. When she was first seen she had the typical distribution of the eruption, and as the eruption spread it seemed to involve the areas of the body not covered by a bathing suit. Her body was not sunburned, and yet where the bathing suit covered the body there is comparative freedom from lesions.

DR WALTER W TOBIN (by invitation). The patient has been tanned all summer, so the condition cannot be due to one exposure to the sun's rays. I appreciate Dr Cornbleet's suggestion concerning estrogenic substance and will try that therapy.

NEW YORK DERMATOLOGICAL SOCIETY

FRANK C COMBES, M D, *President*J GARDNER HOPKINS, M D, *Secretary*

Oct 24, 1939

Lupus Erythematosus Disseminatus Presented by DR HOWARD FOX.

Mrs C C, aged 45, first noticed an eruption while on a sea voyage to Bermuda. The eruption appeared without exposure to strong sunlight, as she did not go on deck during the trip. The lesions are present during the warmer months and disappear almost completely during the winter. They involve the greater part of the face, the sides of the neck, the suprascapular region and the upper part of the chest. They consist of ill defined dull red superficial dry areas covered with a moderate amount of fine adherent scales. There is no apparent atrophy, and there are no subjective symptoms. The hair is sparse, as a result of former lesions in the scalp.

The patient is well nourished and apparently in fair health. The onset of each attack has been accompanied by "bilious" symptoms. She has an occasional rise of temperature, as high as 101 F, lasting a few days.

Urinalysis showed nothing abnormal. The hemoglobin was 60 per cent. A blood count showed 4,700 leukocytes per cubic millimeter, with 65 per cent polymorphonuclear neutrophils. The sedimentation rate of the blood was 73 mm after forty-five minutes.

DISCUSSION

DR FRANK C COMBES I suggest a bismuth preparation, tartro-quinobine, which combines the benefits of iodine, quinine and bismuth in one injection. I have had success in 1 case. Several reports of similar cases have appeared in the literature.

Colloid Milium Presented by DR GEORGE C ANDREWS (by invitation)

C D, a girl aged 9 years, is presented because of a symmetric papular eruption distributed over the nose, forehead and cheeks. The condition began when she was 1 year old, after an attack of gastroenteritis, and was called eczema at that time. The condition persisted and spread, seeming to be a little better in the summer than in the winter. The skin of the affected areas is dry and scales slightly. When it is not oiled regularly, fissures develop. The lesions do not itch, and there are essentially no subjective symptoms. A sister who is younger has a similar condition in a milder form.

Examination shows that the papules are flat, slightly elevated glistening lesions that are thickly studded so as to form a somewhat mosaic pattern, which has been described as resembling kernels of corn on a cob. The lesions are skin colored, slightly lemon or yellow. They vary in size up to several millimeters in diameter. A few papules are umbilicated or suggest the appearance of vesicles.

The chief histologic change was located in the papillary and subpapillary portions of the corium where there were collections of homogeneous material which tinctorially was moderately acidophilic, staining a light red with eosin. Generally these masses were separated from the epidermis by a thin band of connective tissue.

DISCUSSION

DR FRED WISE The other diagnosis which was suggested was lipoidosis cutis. In the reported cases of lipoidosis cutis hoarseness is regarded as a prominent symptom. In this patient there is no involvement of the larynx. Although I should not have been able to make a diagnosis of colloid milium on the clinical

appearance of this patient, I feel that this diagnosis is the most likely. Did any of the cases described as instances of colloid milium resemble this case clinically?

DR GEORGE MILLER MACKEE At first glance the eruption looked like a circumscribed neurodermatitis and made me think of the possibility of amyloidosis. However, on second inspection there seemed to be elementary lesions consisting of tiny nodules or papules. The condition apparently belongs in the class of colloid degenerations. I therefore agree with the diagnosis presented.

DR J. GARDNER HOPKINS I do not think that one should neglect the fact that there has been lipid demonstrated in the skin. Whether that makes this condition distinct from those described as colloid milium is hard to say, as no tests are usually reported.

Leprosy with Juxta-Articular Nodules. Presented by DR FRD WISE

A M, a housewife aged 52, born in Sicily and a resident of the United States for the past twenty-eight years, was seen for the first time by Drs Freeman and Greengrass at the Nathan and Miriam Memorial Hospital in Paterson, N J, on Oct 16, 1939. She is married and has 4 living children, the oldest being 26 and the youngest 12 years of age. There is no history of any abortions. The exact onset of her disease is difficult to establish. It seems to date back twenty-one to twenty-two years. Eleven years ago both hands were clawed and anesthetic to such a degree that in her work as an operator on a winding machine she unconsciously caught her right hand in the machine. As a result of this accident, the distal phalanx of the right middle finger was surgically amputated.

In May 1938 for three weeks she was a patient in the ward at the Paterson City Hospital. The history was irrelevant, and the results of clinical examination and the Wassermann reactions of the blood and spinal fluid were negative, but a diagnosis of syringomyelia and possible late syphilis was made. She was brought to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct 19, 1939, and presented the following clinical picture. There were purplish discolorations of both cheeks. On the wrists and extending up the forearms dorsally were several semicircular scaly lesions with clear centers. The same type of lesion was observed about each knee. In the region of each elbow there were nodules the size of walnuts. A somewhat larger nodule was present below each patella. On each sole there was an open deep ulcer with thickened edges. Both hands were clawed, and there was complete loss of thermal sensation, pain and tactile sensation from the elbows and knees distally in all extremities. Both ulnar nerves were greatly thickened and easily palpated.

Smears made from the open sores were negative for Hansen's bacilli. The Wassermann reaction of the blood was negative. Histologic examination showed findings consistent with the diagnosis of leprosy except that no bacilli were found. Roentgenograms of both hands were normal except for the clawing.

The case is presented chiefly on account of the unusually prominent juxta-articular nodules in both elbow regions.

DISCUSSION

DR HOWARD FOX I have had a great deal of clinical experience with leprosy, but I do not recall having observed a case of either the cutaneous or neural type with juxta-articular nodules such as this patient presents. The lesions resemble the nodes occurring at times in syphilis and yaws.

DR FRANK C COMBES I do not believe any one thinks that these nodules are lepromas.

A Case for Diagnosis (Schamberg's Disease?). Presented by DR J. GARDNER HOPKINS

M L, a woman aged 60, noticed three years ago a brown patch on the dorsum of the right foot which has slowly extended. Similar smaller patches appeared

on the dorsum of the left foot and on the side of the ankle. The lesions are areas of dark brown pigmentation, on the borders of which minute red points can be seen.

DISCUSSION

DR FRED WISE Schamberg's disease is progressive pigmentary dermatosis, usually confined to the foot and toes. The eruption in this patient seems to favor this diagnosis.

DR EUGENE F. TRAUB As both legs pit decidedly on pressure, I would suggest studying the question of circulation. As far as the superficial vascular changes and pigmentation are concerned, I have seen some of these conditions influenced by snake venom injected directly into the lesion. While one can never be certain of the diagnosis of Schamberg's disease, in some cases of dermatitis hemostatica the eruption and pigmentation will disappear completely with such treatment.

A Case for Diagnosis (Poikilodermatomyositis?) Presented by DR J. GARDNER HOPKINS

M. R. B., a stenographer aged 24, eleven years ago noticed the development of white spots in the skin of the forearm. Similar spots appeared in other regions, but there were no other symptoms. In April 1938 she first noticed stiffness of the legs, making it difficult for her to get her heels on the ground when standing in her bare feet. Six months later she began to be troubled with stiffness of the hands which interfered with the use of her bookkeeping machine. She had some paresthesias in the arms at night but no other symptoms. The past history was irrelevant.

Examination shows rather ill defined areas of atrophy with some telangiectasis over the hips and buttocks and faint white atrophic spots on the arms and legs suggestive of anetoderma. On the back of the left foot is a band of skin which feels stiff and is reddened and slightly hyperkeratotic. The muscles of the calves and forearms seem somewhat indurated. Flexion of the ankle is limited. There is slight puffiness of the hands, and the fingers cannot be completely closed.

The results of general physical examination were negative. Blood and urine examinations were normal. Roentgenograms showed no changes in the bones or joints and no subcutaneous calcification.

The case is presented as one of possible incipient poikilodermatomyositis.

DISCUSSION

DR HOWARD FOX In one area the lesions seemed to me to be typical of morphea guttata. In another area there was a patch of apparent morphea en bande.

DR EDWARD R. MALONEY I agree with the diagnosis of morphea made by Dr. Fox.

DR R. H. RULISON I saw this patient four or five years ago. I do not recall much about the case, but I remember that at that time she had no interference with the musculature and only slight lesions on the arms.

DR J. GARDNER HOPKINS I should like to know if morphea can be associated with muscular changes. Symptomatically the patient has limitation of motion of the hands and feet.

DR GEORGE MILLER MACKEE Is not the slight limitation of motion caused by the possible scleroderma?

DR EUGENE F. TRAUB I agree with Dr. Fox that the eruption is in all probability morphea.

DR J. GARDNER HOPKINS The condition does not seem to me to be hidebound, certainly not over the hands, and a band in the front part of the leg would not interfere with flexion of the foot.

Congenital Fragilitas Crinium Presented by DR EUGENE F TRAUB

D N, a woman aged 21, states that her entire family had good scalp hair, as far as she knows, and that she has always had a growth of hair over the scalp. At no time has the hair on her scalp fallen out entirely, but neither has it grown longer than a short boyish bob, in other words, her hair measures about 4 or 5 inches (10 to 12 cm) at its maximum length. At the ends some hairs seem to split. The hair is dry, rather lustreless and brittle. The patient has always enjoyed good health, and her only complaint is the fact that the hair does not grow long.

DISCUSSION

(The members accepted unanimously the diagnosis presented.)

Bourneville-Pringle Syndrome Presented by DR. EUGENE F TRAUB

M. K, a woman aged 32, is presented as having the Bourneville-Pringle syndrome. This syndrome, which consists of tuberous sclerosis, adenoma sebaceum, Recklinghausen's disease and subungual fibromas, may perhaps not be represented in all its details in this patient. The striking feature of the case is the presence of subungual fibromas on practically all the toes and on a number of the fingers. The adenoma sebaceum on the face is also well marked, especially about the nasolabial angles, where there are numerous small nodules with relatively little increase in vascularity (telangiectasia). A few scattered fibromas on the trunk suggest abortive Recklinghausen's disease, but there is no evidence for or against tuberous sclerosis.

DISCUSSION

DR EUGENE F TRAUB: Have the members any suggestions as to what to do about the subungual fibromas? I have removed a few of them. Is it safe to remove them?

DR. GEORGE MILLER MACKEE: I think that it would be safe to remove the subungual fibromas.

A Case for Diagnosis (Pemphigus Erythematodes?). Presented by DR EUGENE F TRAUB

E S., a man aged 47, was previously presented for diagnosis before this society in April 1939 (*ARCH DERMAT & SYPH.* 40:1039 [Dec] 1939). At that time the diagnoses considered were pemphigus and seborrheic eczema. At the present time a definite clinical diagnosis of some type of pemphigus can readily be made. The only question now is whether the patient has pemphigus vulgaris or the so-called Senear-Usher type of pemphigus. He spent three weeks under the care of Dr U. J. Wile, who was not certain of this point, but I believe that he favored the latter type.

DISCUSSION

DR HOWARD FOX: I saw this man in consultation and took a specimen of blood for a Pels-Macht test. The report was 59 per cent toxic, which is the reading for pemphigus.

NOTE—Since the date of presentation this patient died in his automobile of carbon monoxide poisoning.

A Case for Diagnosis (Actinic Atrophy?). Presented by DR J GARDNER HOPKINS

W. P. R., a physician aged 35, about five years ago noticed reddish patches on each side of the neck below the ear, which have slowly increased in intensity and extended. The patches are ill defined and brownish red. On close inspection, they are made up of reticular dull red depressed lines in the lesions of which the sebaceous follicles stand out as islands of white in apparently normal skin.

Histologic examination showed a mild atrophy with some telangiectasis, without distinctive changes

DISCUSSION

DR PAUL E BECHET This clinical picture is extremely common and presents little, if any, variation. It is seen most frequently in men who have been excessively exposed to actinic light. As a rule the condition is so common that the patient does not bother about therapy. I do not believe that there are any radical differences between poikiloderma of Civatte and actinic dermatitis. In fact, I strongly suspect that they are identical.

DR HOWARD FOX The condition looks to me like mild poikiloderma of Civatte. As this young physician seems concerned over the appearance of the lesions, I suggest using a light desiccating spark for cosmetic purposes.

DR FRED WISE My impression is that this condition is ordinary weather-beaten skin of the neck, which is prevalent especially in men leading an out-of-door life.

DR FRANK C COMBES I agree with Dr. Wise but do not see why this particular location is chosen for the reaction. In the sun a person gets a burn usually on the forehead, and this reaction never occurs on the forehead. Therefore, I think there is some other factor responsible for this type of atrophy.

Granuloma Annulare (Left Leg) Presented by DR EUGENE F. TRAUB

G. L., a woman aged 31, was first seen in June 1939, with an eruption on the left leg of four years' duration. Examination shows a purplish pink circinate lesion with a clear atrophic center and a slightly scaly border which, while elevated, does not seem to consist of distinct papular lesions but fades into the surrounding skin. The lesion is located on the inner aspect of the left leg. There is some slight wrinkling of the skin in the center of the lesion, which is interpreted by the presenter to be atrophy.

Histologic diagnosis was granuloma annulare. The section showed atrophic epidermis, and scattered throughout the corium were islands of cellular exudate, which were grouped about islands of swollen collagen fibers. The cellular exudate consisted of lymphocytes and giant cells of the Langerhans type, as well as numerous plasma cells. The Weigert stain showed some slight variations in the elastic tissue fibers. In the area of the lesion, the elastic tissue fibers were swollen, and the changes in the collagen fibers showed definitely some of the degeneration seen in granuloma annulare.

The Wassermann and Kahn reactions were negative. The sugar content of the blood was 80 mg. per hundred cubic centimeters. Tuberculin tests with dilutions of 1:1,000,000, 1:100,000 and 1:10,000 gave negative results.

The patient has received up to the present time six roentgen ray treatments, one-half skin unit (150 r), unfiltered, to the area, with some improvement.

DISCUSSION

DR EDWARD R. MALONEY Apparently the histologic examination shows granuloma annulare to be the diagnosis. Clinically the condition looks enough like granuloma annulare to make that diagnosis, but I would call it atypical. Certainly the center of the lesion does not look much like the center of the ordinary lesion of granuloma annulare.

DR PAUL E. BECHET I should like to ask whether the present flat appearance of the lesion is due to treatment by Dr. Traub or by some one else.

DR FRANK C. COMBES I think that the duration of the lesion and the atrophy in the center are uncommon in this condition.

DR EUGENE F. TRAUB I presented the patient because I thought probably there would be some disagreement with the diagnosis. When the specimen was

sent to the laboratory, a number of diagnoses were suggested, including granuloma annulare. However, at no time did I think that the border of the lesion was the usual type seen in that disease, and I have never seen granuloma annulare with a central portion that looked atrophic as this does. Of course, there may be some question as to whether there is actually atrophy in the center, but assuming that it is and considering the peculiar border, I do not see how a diagnosis of granuloma annulare could be made clinically. I am willing to accept it only if the histologic picture is considered definite, as it was in the laboratory of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

Recurring Lichen Planus Presented by DR HOWARD FOX.

Mrs. I. P., aged 46, born in Finland, is now suffering from the fourth attack of the ordinary type of lichen planus, each of which I observed. The eruption appeared first in May 1925, the active lesions disappearing at the end of four months. The second attack began in April 1928 and lasted nine months. The third attack appeared in April 1935 and lasted five months. The present attack began about four months ago. The location of the eruption has always included the favorite sites of the disease. The disappearance of active lesions has been followed, after each attack, by temporary pigmentation, eventually disappearing without trace. In addition to the typical lesions of ordinary lichen planus, she has suffered for the past four years from small patches of the hypertrophic type situated on the shins.

She has been treated by roentgen and by ultraviolet radiation and with injections of enesol (mercuric salicylarsenate). The patient is well nourished and in apparent good health.

DISCUSSION

DR HOWARD FOX. On the same day that this woman consulted me, I saw another patient who had had three attacks of lichen planus in the past twenty-five years. Last year I also saw a man who was suffering from the third attack of this disease in a period of about twenty-five years.

Sarcoidosis Presented by DR FRANK C. COMBES

A R., a Negress aged 33, was admitted to Bellevue Hospital in July 1939, with a generalized eruption of six years' duration. In 1934 she received about fifty intravenous and intramuscular injections for syphilis, without any effect. The Wassermann and Kahn reactions of her blood have been repeatedly negative, and the spinal fluid has been normal. On admission her eruption was essentially as it is now except that it was more inflammatory and the lesions were covered with a thick rupioid crust, surmounted in many instances on a micaceous scale. The eruption is generalized, sparing her soles, palms and scalp. There are two types of active lesions, one a pea-sized to bean-sized smooth elevated nodule and the other, an irregular, sharply defined dusky red nonelevated patch varying up to 10 cm in diameter. Many of these are bizarre in outline, with some circinate and others reniform or dumbbell shaped. In the center of these lesions the skin is lighter in color and atrophic, representing the healed process. On the left cheek, extending anteriorly to the ear, is a linear keloid scar, although at no time have any of the lesions ulcerated. There is also some shrinkage of the skin at the tip of her nose, especially of the nostril. She has general adenopathy.

The blood count and chemical examination gave negative results except for evidence of moderate secondary anemia. The tuberculin test was negative with a 1:1,000 dilution. Roentgenograms showed interstitial changes and fibrosis at the roots of both lungs extending to the bases. Multicystic changes were present in the bases of the right first and second metacarpal bones and in several of the carpal bones. The bones of the feet and skull showed no gross pathologic changes. Histologic examination showed lupoid structure.

DISCUSSION

DR EDWARD R MALONEY The clinical diagnosis one would make here is tuberculosis of the skin. There are scars on the neck which are characteristic of scrofuloderma. In spite of the histologic report of lupoid structure, a histologic examination was done by Dr Riordan, and he told me that the condition was lupus vulgaris. The pulmonary changes one would find in 50 per cent of normal people. The bony changes are so hard to make out that I doubt if there are any. In sarcoidosis pulmonary and bony changes are the prominent features, and the cutaneous changes are slight. There are two types of sarcoid, one type being tuberculous and the other, nontuberculous. I think that here there is a superficial tuberculosis of the skin, a low grade infection. The one point against that diagnosis, to my mind, is the fact that the patient gave a negative reaction to a tuberculin test, but she may have enough anticutanes to bring about that result.

DR PAUL E BECHET I think one of the things which might cloud the issue in the diagnosis of sarcoidosis and the diagnosis of tuberculosis in this particular patient is the fact that she is a Negress. For some reason unknown to me, the manifestations of tuberculosis are so varied and so protean in Negroes that it is much more difficult to make the diagnosis than in white persons. However, I believe this case is definitely one of tuberculosis of the skin.

DR J GARDNER HOPKINS I should like to agree with both Dr Combes and Dr Maloney, because, as I understand it, one view of sarcoidosis is that it is tuberculosis of the skin with absence of necrosis, the latter probably being due to the fact that the patient is not sensitive to tuberculin. I saw no necrosis, ulceration or scarring in any of the lesions in this patient.

DR EDWARD R MALONEY If Dr Hopkins had examined the patient closely I am sure he would have seen definite scarring in the neck.

DR JEROME KINGSBURY In a case like this I believe that syphilis should be definitely ruled out. According to the history, as I understand it, all the lesions appeared at the same time, and their configuration and distribution is that which might be seen in one of the atypical syphilids that even now occasionally occur in Negroes. None of the present lesions are active ones. They contain scar tissue, show pigmentary change and are, I believe, the end result of preexisting lesions of a different character.

DR GEORGE MILLER MACKEE It is, of course, possible to have more than one variety of tuberculosis and tuberculid in the same patient. In line with what Dr Maloney and other speakers have said, scrofuloderma might account for the keloidal scars on the neck, and it is conceivable that there might have been a nodular lesion which looked clinically and microscopically like lupus vulgaris. That might account for the report which Dr Maloney received. Finally, the patient might also have a low grade tuberculosis, namely, sarcoid. The changes in the bones were difficult to make out, it is true, but they were definite. One bone showed three distinct areas of atrophy.

DR FRANK C COMBES I think that syphilis can be eliminated. If the condition were syphilis, it would be an early tertiary or late secondary syphilid, and the Wassermann reaction would in all probability be positive. I cannot conceive of any early or late secondary eruption of such extent with a negative serologic reaction. If the condition were a late secondary syphilid, one would not see scarring such as is present in this case. As far as Dr Maloney's remarks are concerned, I agree with him. I will accept this case as one of hematogenous non-caseating tuberculosis of the skin, and if it is that, then it is sarcoid. One point against the diagnosis of tuberculosis of the skin is the total absence of caseation and the tuberculin hypoergy. The patient responded to pure tuberculin but not to a 1:1,000 dilution. The spontaneous healing of the lesion without treatment, I think, is against this being actual tuberculosis of the skin. One can conceive of the whole process as tuberculosis with an exceptionally high degree of tissue immunity which produces a tuberculoid or sarcoid structure instead of the ordinary structure of lupus vulgaris or ordinary disseminated tuberculosis cutis.

Unilateral Acneform Eruption (Following Use of Cold Cream). Presented by DR. FRANK C COMBES

Y L, a woman aged 19, was first seen at the dermatologic clinic of Bellevue Hospital in August 1939, with an eruption on her face. Four months ago she had Bell's palsy of the left side of the face, for which she applied a cold cream and vibratory massage. After three daily treatments the left side of her face became inflamed and covered with closely set miliary pustules and comedos. These were confined entirely to the area treated, the right side of the face being clear. Treatment consisted of application of white lotion N F, to which she responded in about six weeks. At present she shows profuse reticulated pitted scarring confined to the left side of the face, stopping abruptly at the midline of her forehead and chin.

DISCUSSION

DR GEORGE MILLER MACKEE. This is a puzzling case. It is inconceivable that such a simple thing as cold cream or petrolatum could produce acne vulgaris. I would be inclined to classify the condition as a follicular pyoderma, with acneform lesions due probably to infection of those follicles at the time of the treatment with pyogenic organisms.

DR JEROME KINGSBURY. I agree for the most part with Dr MacKee's conception of the case. It does not seem at all likely that the condition could have been caused by the application of cold cream or any other simple emollient. It is more probable that a folliculitis might have resulted from the employment of some depilatory used for hirsuties.

DR FRANK C COMBES. Of course, one can easily fall into error in a case such as this, by misinterpreting cause and effect. The patient ascribes the eruption to the use of cold cream. It is possible, of course, that infection followed its use but not probable. It is difficult to conceive of such an infection being limited to one side of the face. Why should it not spread? The condition has none of the earmarks of rosacea-like tuberculosis of the skin. I may be able to perform a biopsy, but I think it would be advisable to wait, as a lot of the redness will eventually disappear.

Lupus Vulgaris. Presented by DR FRANK C COMBES

C W, a woman aged 57, was admitted to Bellevue Hospital in 1936. The only significant elements in the previous history are a duodenal ulcer in 1935, which responded to medical treatment, and a thyroidectomy in December 1938 for toxic adenoma. Physically her condition is good, although her weight is only 88 pounds (39.9 Kg). The Wassermann reaction was negative, and the urinalysis gave normal results. Roentgenographic examination of the gastrointestinal tract showed a duodenal ulcer. Roentgenograms of the lungs show fibrosis of the bases of both lungs. The results of tuberculin tests were positive with a dilution of 1:1,000,000.

On her face in "butterfly" configuration over her nose and both cheeks is a well defined infiltrated nodular plaque of ten years' duration. Throughout the lesion there is evidence of atrophy, but there is no ulceration. The borders are raised, and diascopic examination shows typical apple jelly tubercles.

The patient has had forty-three treatments with the air-cooled quartz mercury vapor arc lamp plus a salt-free diet and administration of gold sodium thiosulfate, with little benefit.

DISCUSSION

(The members accepted unanimously the diagnosis presented.)

A Case for Diagnosis (Senear-Usher Pemphigus? Dermatitis Medicamentosa?). Presented by DR FRED WISE

J P, a woman aged 47, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, with an eruption of five months'

duration The eruption is distributed over the scalp, the upper anterior and posterior surfaces of the chest, the neck posteriorly and laterally and the arms and forearms, especially on the extensor surfaces On the anterior surface of the chest there are grouped silver dollar-sized patches of recent origin at the sites of healed lesions Here also are two active erythematous, somewhat violaceous lesions with pea-sized superficial central erosions Spreading across the entire upper part of the back is a similar process, which does not consist of single lesions but presents an upper raised scalloped border with moderate erythema, below which it gradually fades to a similar depigmented zone Below the posterior hair line on the neck are smaller nummular, violaceous lesions, somewhat crusted, with central erosions There are a few disseminated pea-sized moist lesions with yellow friable crusts on the scalp On the arms and forearms are smaller lesions, similar to those on the neck, in the stage of regression

Within the past two weeks there has been considerable improvement in the appearance of the eruption Whether this is the result of the discontinuation of ingested sedatives (elixir of alurate) is not yet determined The medication had been prescribed for insomnia by physicians in the department of neurology, where a diagnosis of involutional melancholia had been made

Urinalysis showed many tiny calcium oxide crystals, many pus and epithelial cells and large quantities of amorphous urates

Histologic examination (by Dr D L Sateuistein) indicated a superficial exudative dermatitis

DISCUSSION

DR R H RULISON I suggest tentatively that this condition might be mycosis fungoides

DR GEORGE MILLER MACKEE Partly because of the patient's mental condition and partly because of the fact that, although the eruption is fairly generalized and not easy to reach, there is not a lesion that the patient could not cause herself with phenol, I suggest the possibility of malingerer

DR HOWARD FOX Against the diagnosis of a factitious causation is the fact that this eruption is fairly symmetric on both sides of the chest and back and is in a region which is difficult for the patient to reach

DR EUGENE F TRAUB This patient presents a configurate eruption on the back which, it seems to me, would be exceedingly difficult for her to produce, although I had this possibility in mind when I examined her The lesions on the chest might conceivably have been produced by the patient I believe the possibilities are as Dr Wise outlined them My feeling is that the condition is most likely a drug eruption because of the appearance of some of the lesions well up in the scalp and on the back of the neck

Lichen Planus with an Annular Lesion on the Scalp Presented by Dr EUGENE F TRAUB

J S, a woman aged 39, was first seen on Oct 13, 1939 The striking feature of the eruption was the peculiar eruption on the face and the annular lesions on the scalp, with one on the lower lip She has a peculiar mottled, brownish red telangiectatic area on the tip of her nose which, I feel, is probably part of the lichen planus The generalized eruption on the trunk is typical lichen planus

Two biopsies were performed One specimen, which was taken from her right arm, was reported as lichen planus The section showed an atrophic epidermis covered with a thick scale, with irregular thickening of the granular layer There were edema and some pigmentation in the upper part of the corium Because of the unusual appearance of the eruption on the face and the telangiectasia, the second piece of skin removed for study was taken from the forehead This was reported as showing an inflammatory stage of lupus erythematosus The section showed an atrophic epidermis with a nonparakeratotic scale There was a perivascular

exudate scattered throughout the entire corium, as well as dilated blood and lymph spaces. There was granular edema of the collagen fibers, and some of the fibers took a basophilic tinge. There was a slight amount of pigment. Elastic tissue stain showed beginning degeneration of the fine elastic tissue fibers.

DISCUSSION

(The members accepted unanimously the diagnosis presented.)

A Case for Diagnosis (Pemphigus? Lupus Erythematosus Bullosus?).

Presented by DR EUGENE F TRAUB

I M., a man aged 45, born in the United States, was first seen in December 1930, with an eruption confined to the roof of the mouth of one year's duration. The patient was previously presented before this society in November 1934 and in February 1935 (ARCH DERMAT & SYPH 32:978 [Dec.] 1935).

Repeated smears for Vincent's angina have been negative. The patient presents an irregularly shaped ulcer suggesting either a syphilitic process or a tuberculous ulcer. Repeated Wassermann reactions have been negative, and injections of neoarsphenamine and a bismuth compound have had no effect on the process. A roentgenogram of the chest was normal. Blood counts have been repeatedly normal. No monilia or any other organism was found. A complete investigation was carried out in the department of allergy, and the patient was given scratch tests for all types of grasses and pollens, all foods, a routine group of twenty-nine chemicals and miscellaneous epidermals. Urinalysis gave negative results. Smears taken from the nose, throat and stools showed only a few hemolytic streptococci. Four biopsies were performed on the mucous membrane lesion of the mouth, with reports of "inflammatory nodule" or "chronic inflammatory nodule."

The patient has received numerous injections of vaccine and gold therapy, in addition to the bismuth compound and arsenic before mentioned.

DISCUSSION

DR FRED WISE Kummer, of Germany, has published reports of cases of this kind and has stated the belief that the conditions are caused by the virus of herpes simplex. I suggest that this patient receive a course of ordinary cow pox vaccinations. I also suggest the inoculation of a rabbit's cornea with the secretions obtained from some of the active lesions to determine whether the virus of herpes simplex is present.

Acanthosis Nigricans. Presented by DR FRED WISE

S C., a man aged 31, is presented for Dr J J Greengrass

DISCUSSION

DR HOWARD FOX. As the eruption first appeared in childhood, it should be classed as an example of the juvenile type of acanthosis nigricans. The prognosis should be good. I should like to ask the members whether any one has followed such a case for a long period of time.

DR J GARDNER HOPKINS. Is there any history of cancer in the family? Dr Curth has found a high incidence of cancer in the families of patients with "benign" acanthosis nigricans.

DR FRED WISE. I was unable to obtain any history relating to benign or malignant tumors in this patient's family.

DR HOWARD FOX. An unusual clinical feature is the presence of large numbers of lesions that look like pigmented nevi and cutaneous tags of various sizes. The presence of these lesions is most unusual in my experience.

DR FRED WISE. The coexistence of scattered pigmented moles and nodular tumors is not uncommon in acanthosis nigricans.

Report on a Case of Ulcer of the Tongue By DR PAUL E BECHET

R S, a man aged 47, was presented before the Manhattan Dermatologic Society on March 14, 1939 (ARCH DERMAT & SYPH 40 623 [Oct] 1939), for diagnosis (ulcer of the tongue), with tentative diagnoses of syphilis, tuberculosis or carcinoma. The patient was presented on the day of his admission to the clinic.

Dr MacKee is to be congratulated on his clinical diagnosis of tuberculosis. The subsequent work done on this case has established definitely that the lesion on the tongue is tuberculosis. Roentgenograms of the lungs showed tuberculosis. One odd finding was that the tuberculin tests gave negative results with various dilutions. Histologic examination showed tuberculosis. It is strange that the patient has lost no weight. He has, in fact, gained 8 pounds (3.6 Kg) and seems in perfect health.

CLEVELAND DERMATOLOGICAL SOCIETY

C L BASKIN, M D, *President*, Akron, Ohio

C G LA ROCOCO, M D, *Secretary*

JAMES R DRIVER, M D, *Reporter*

Oct 26, 1939

Urticaria Pigmentosa. Presented by DR HAROLD N COLE and DR J R DRIVER

R G, a boy aged 19 months within one month after birth had a generalized eruption which has persisted in spite of various forms of therapy. Because of the pigmented character of the eruption and the presence of lesions on the palms and soles, syphilis had been considered as the probable diagnosis by the attending physician. The child is well developed and well nourished.

Distributed over the trunk and even on the palms and soles is a generalized macular pigmented (reddish brown) eruption. The primary element seems to be an elongated macule with a slightly irregular shape. Most of the macules are about the size of a split pea. On the back there are some urticarial lesions with reddish halos. Some of the areas show a suggestion of infiltration or edema. The mucosae are normal.

Serologic tests for syphilis gave negative results.

DISCUSSION

DR HAROLD N COLE. This case is shown, first, because it presents a splendid example of this rather rare dermatosis, and secondly, because in this particular case a diagnosis of syphilis had been made by the family physician.

DR GEORGE H CURTIS (by invitation). I should like to suggest that the child would be an excellent subject for a colored photograph. The condition would show up beautifully.

Hemochromatosis with Diabetic Bronzing Presented by DR H H JOHNSON

W S, an unemployed die maker, aged 61, presented from the department of dermatology and syphilology, Lakeside Hospital, was first observed in the outpatient department of the University Hospitals in April 1932, with a history of diabetes for three years. Somewhat later it was noticed that the "tan" that developed on his face and forearms was dull and grayish. In September 1932 the edge of the liver was palpable 3 fingerbreadths below the right costal margin in the mid-

clavicular line There was bilateral arcus senilis, and there were slight lenticular opacities The skin of the face, neck, hands and forearms presented a dull gray pigmentation with superimposed brown lentigo The blood sugar was 261 mg per hundred cubic centimeters, and the blood cholesterol, 204 mg per hundred cubic centimeters The diabetes was fairly well controlled at that time In 1935 he was admitted to the medical service of Lakeside Hospital with diabetic acidosis and with the liver descending within 15 cm of the umbilicus In 1936 he was readmitted, because of repeated insulin shocks Liver function tests showed a weakly positive Takata-Ara reaction The urea nitrogen content of the blood was 13.5 mg per hundred cubic centimeters, and the nonprotein nitrogen content, 35 mg per hundred cubic centimeters, with a ratio of 0.38 The serum phosphorus was 6 mg per hundred cubic centimeters He was readmitted in November 1938, when the icteric index was 7 The bromsulphalein test showed 45 per cent retention in seven minutes and 5 per cent retention in thirty minutes A galactose tolerance test (with 40 Gm of galactose) showed that the blood sugar rose from 216 mg to 425 mg per hundred cubic centimeters two and one-half hours after administration

Physical examination shows a dry skin with slight scaling on the forearms and the lower thirds of the legs There is a moderate diffuse grayish brown pigmentation of the skin of the forearms, hands, lower thirds of the legs, face and neck, most marked on the dorsa of the hands and the lower thirds of the legs There are a few lentigines on the forearms and hands There is an arcus senilis, and there are minimal lenticular opacities

The edge of the liver was palpable 5 cm below the right costal margin in the midclavicular line; the liver was firm and smooth, with a somewhat rounded edge

There was glycosuria, and the blood sugar was 216 mg per hundred cubic centimeters The hemogram was not remarkable Serologic tests for syphilis gave negative results

Histologic examination of skin on Sept 22, 1932, showed scattered small aggregations of finely dispersed brown pigment in the stratum germinativum of the epidermis, in the corium and even in the deeper connective tissue, especially around the sudoriparous glands Iron stains showed this pigment to be iron containing

DISCUSSION

DR HAROLD N COLE. I should like to mention something that is not really pertinent When Dr T. B Mallory was here a number of years ago and gave a talk on this subject—of course, he was the exponent of the copper intoxication theory—Dr A. I Ludlow heard the lecture He made the comment that it is strange that there is no diabetic bronzing in Korea, where everything is cooked in a copper kettle

Keratoderma Palmare et Plantare Hereditarium Punctatum. Presented by DR H H JOHNSON

H S, a man aged 34, presented from the department of dermatology and syphilology, Lakeside Hospital, has had "warty" growths on his palms and soles as long as he can remember There have been no associated symptoms The patient's father and sister both have similar lesions, and similar lesions are developing in his daughter, aged 3 years There was no history of ingestion of or trade exposure to arsenic

There are several yellowish translucent hyperkeratotic papules, 2 to 4 mm in diameter and elevated about 2 mm above the surface, on the palmar aspects of both hands and on the plantar aspects of both feet

Histologic examination showed stratified squamous epithelium of varying thickness, above which there was a thick layer of basophilic keratohyaline material

The corium was dense and contained a few sweat glands and several structures which appeared to be abortive hair follicles

DISCUSSION

DR JOHN GAMMEL It would be interesting to know whether the other members of the family who have this condition also have the punctate lesions

DR OTTO SCHMIDT (by invitation) All the members of the family mentioned in the history have the same type of involvement

DR HAROLD N COLE The punctate type of keratoderma is much rarer than the ordinary diffuse type I doubt if more than 5 per cent of such cases are of this variety

Pemphigus Erythematodes (Senear-Usher Syndrome). Presented by DR H H JOHNSON

E R, a Jewess aged 53, presented from the department of dermatology and syphilology, Lakeside Hospital, entered the outpatient department of the hospital on July 1, 1938, with slightly pruritic exuding erosions beneath the breasts and about the ears and vesicular lesions about the waist and over the spine, which persisted in spite of local therapy On September 20 she was admitted to the hospital with the additional complaints of headaches, chilliness and dizziness of three weeks' duration

Physical examination on admission showed many superficial, slightly oozing erosions, surrounded by an area of moderate erythema, on the face and trunk and several vesicles and bullae on the abdomen The Nikolsky sign was repeatedly present

Except for a white blood count of 10,000 per cubic millimeter, with 15 per cent eosinophils, the hemogram was normal The urine was normal

The patient had a low grade fever throughout her hospital stay of thirty days, reaching 38 C (100.4 F) daily When treated with local astringents and antiseptics the condition remitted, and the lesions were nearly healed on discharge

Her skin was clear until Jan 15, 1939, when a scaling, moist lesion developed on the right cheek, with definite follicular plugging The lesion persisted unchanged, and on July 5 several new crusting and scaling lesions were noted on the face In August she received three roentgen treatments of 75 r each to the face, but the lesions progressed On August 30 she was given an injection of bismuth subsalicylate and has received eight weekly injections (0.2 Gm each) to date without improvement A blood count was made on October 23, showing 5,200 leukocytes per cubic millimeter, with 10 per cent eosinophils

DISCUSSION

DR J EDGAR FISHER I agree with the diagnosis as presented The patient presents typical signs of the Senear-Usher syndrome

DR H A HAYNES JR I suggest trying sulfanilamide in this case

DR H H JOHNSON May I ask on what basis that is suggested?

DR H A HAYNES JR A purely empiric basis

DR H H JOHNSON When the patient was first observed with a bullous eruption, there was a great deal of dispute as to whether the condition was pemphigus or dermatitis herpetiformis Most observers concurred in the diagnosis of pemphigus The eruption disappeared, and there later developed an isolated lesion of the sort present now The lesion as seen now both pathologically and clinically would pass as discoid lupus erythematosus

DR J R DRIVER I think that no one who saw this patient at the start would have suggested a diagnosis of the Senear-Usher syndrome The appearance was more or less typical of pemphigus A transformation has occurred,

and now I believe all agree with the diagnosis of Seneear-Usher syndrome (pemphigus erythematodes of Ormsby) Transitions of this type have been reported on several occasions

Granuloma Inguinale of the Vaginal Wall and Rectum with Profuse Hemorrhage. Presented by DR H H JOHNSON

M M, a Negress aged 28, is presented from the department of dermatology and syphilology, Lakeside Hospital. A reddish vaginal discharge developed in July 1931, three years after surgically induced menopause. On Feb 24, 1933, the urethral floor was thickened, and a deep ulcerated area with a flap of red thickened granulation tissue was seen on the right vaginal wall. The Frei test gave a negative result at that time, and the reaction to a tuberculin test had been negative in April 1931. The lesion failed to heal, and on May 4, 1934, histologic examination was made. The report was of granulation tissue, but the pathologist remarked on the presence of many large indeterminate types of cells with irregular chromatic nuclei. The patient attended the outpatient department irregularly, and the ulceration and bloody discharge continued until Aug 1, 1937, when she was admitted for profuse vaginal bleeding, with a red blood cell count of 2,600,000 per cubic millimeter and 45 per cent hemoglobin. In March 1938 granulosomatous tissue was found in the lower portion of the rectum, resulting from straining at stool. The stools were blood streaked. Since July 1938 she has become progressively weaker and was readmitted to the hospital on Aug 29, 1939.

Secondary syphilis was diagnosed in 1928, with a mucocutaneous relapse in 1932. Inadequate irregular treatment has been received since that time.

On admission to the hospital the temperature was 38.5 C. On the left anterior vaginal wall there was a soft smooth elevated beefy red mass, with ulceration and surrounding scarring. There were many superficially ulcerated granulomatous masses in the lower part of the rectum. The perianal skin and labia showed lymphedema. Profuse hemorrhages have required two blood transfusions.

There were 3,070,000 erythrocytes per cubic millimeter, and the hemoglobin was 35 per cent. The Frei test gave a negative result (with mouse brain antigen). Serologic tests for syphilis gave positive results.

Histologic examination of tissue removed from the vagina in 1934 showed the specimen to consist of dense, fibrous connective tissue, with a moderate degree of lymphocytic infiltration and with several areas heavily laden with monocytes. The Giemsa stain showed purple-staining small spherical bodies in the monocytes.

The patient was given fuadin (sodium antimony biscatechol disulfonate) and to date has received 30 cc. There is a slight regression of the vaginal lesion.

DISCUSSION

DR J R. DRIVER: This case of granuloma inguinale is the first one that I have observed in which there was severe hemorrhage requiring the use of blood transfusions. The case is most unusual.

DR H H. JOHNSON: An interesting fact about this case is that a biopsy was performed in 1934, and the pathologists remarked on the unusual nuclei in the granulation tissue. Had the diagnosis been made at that time, treatment would probably have prevented the hemorrhages that subsequently occurred.

DR HAROLD N COLE: This patient shows a picture that makes one think of the anorectal syndrome of lymphogranuloma venereum. The edema of the labia majora that is present along with the process around the anal orifice would pass for esthiomene, however, this condition is not lymphogranuloma venereum but granuloma inguinale. We have photographs of several patients observed in the past who had granuloma inguinale, yet on looking at these photographs one would say the condition was also esthiomene. I notice a paper is to be read

at the American Academy of Dermatology and Syphilology in November on esthiomene due to granuloma inguinale I have doubted for some time that esthiomene was due solely to lymphogranuloma venereum I believe that it is possible also for the disease to be due to granuloma inguinale, and this case seems to be an example of it

DR GEORGE W BINKLEY The group at the University of Georgia has been working on granuloma inguinale They started about three years ago The first paper was on chancroid by Greenblatt and Sandeison (Greenblatt, R B, and Sanderson, E S Diagnostic Value of the Intradermal Chancroid Test, *ARCH DERMAT & SYPH* 36 486-493 [Sept.] 1937) and in that they showed some slides of pseudobubo of granuloma inguinale I was doubtful about it and did not believe that the disease invaded the lymphatics, but they have carried on their work both in the clinic and on hospital patients and have been able to show that after a certain incubation period they do get a subcutaneous abscess which they call a pseudobubo The aspirated fluid contains Donovan bodies They have tried to grow Donovan bodies on artificial culture mediums, using various serums, but have never succeeded, so Greenblatt was emphatic in his opinion that there is no bacillus such as had been described by Goldzieher and Peck (Goldzieher, M, and Peck, S M Granuloma Inguinale, *ARCH DERMAT & SYPH* 14 14 [July] 1926) The group at the University of Georgia has also shown that the condition is not strictly a cutaneous disease but that it also involves the internal organs A case was reported (Pund, E R, and Gotcher, V A Granuloma Venereum [Granuloma Inguinale] of the Uterus, Tubes and Ovaries *Surgery* 3:34-40 [Jan.] 1938) in which the fallopian tubes were involved and from which Donovan bodies were demonstrated There are apparently many more cases in the South than in this section of the country

DR GEORGE H CURTIS (by invitation) I should like to ask about the terminology for the two diseases under discussion What are the accepted names at the present time?

DR HAROLD N COLE I believe that the accepted terms are granuloma inguinale and lymphogranuloma venereum

DR JOHN E RAUSCHKOLB Both terms are incorrect, because in the original case of Hellerstrom the lesion was a lymphogranulomatous bubo in the axilla of a surgeon These diseases are not necessarily venereal

Arsenical Pigmentation and Keratosis of the Palms and Soles in a Patient with Chronic Myelogenous Leukemia Presented by Dr OTTO E L SCHMIDT

M H, a man aged 43, presented from the department of dermatology and syphilology, Lakeside Hospital, complained of daily chills for ten days He had been admitted to the hospital in April 1938 for treatment of a carbuncle Examination at that time showed that he also was suffering from chronic myelogenous leukemia associated with a huge spleen and an enlarged liver He was given solution of potassium arsenite in doses of 8 drops three times a day This resulted in a change in the white blood cell count from 357,000 (with 44 per cent myelocytes) to 60,000 per cubic millimeter He continued the use of the arsenical preparation under a private physician's care and reentered Lakeside Hospital on May 25, 1939, with a chief complaint of chills and fever He was found to have empyema, and, incidentally, it was noted that the skin generally was dark brown and that the soles showed hyperkeratosis and scaling Solution of potassium arsenite in the original dose was continued, and the white blood cell count was controlled at a level of 10,000 to 20,000 per cubic millimeter

In September he was readmitted to the hospital, for treatment of malaria The arsenical medication had continued uninterrupted since his first hospitalization, a period of approximately seventeen months

Physical examination now reveals him to be a worn, poorly nourished man, whose skin is dry, cool and fairly uniform grayish brown. Scattered over the entire body are innumerable tiny macules, 1 to 2 mm in diameter, paler than the general dark hue of the skin. On both palms are shiny flat areas of hyperkeratosis, but the palmar skin is not generally thickened. Both soles present a yellowish scaly hyperkeratosis.

A recent hemogram showed 70,100 white blood cells per cubic millimeter, with 20 per cent myelocytes and 1 per cent myeloblasts.

DISCUSSION

DR HAL ELSON FREEMAN Is this fine macular pigmentation common in cases of arsenical intoxication, or is the eruption usually larger or more diffuse?

DR HAROLD N COLE I think that it is not uncommon to see this type of pigmentation in connection with the ingestion of arsenic over a long period. I remember seeing a girl some years ago who had been taking an old-fashioned prescription for chronic constipation over a long period. She not only had arsenical keratoses on the palms but had this same type of pigmentation all over the trunk even more extensively than this patient has.

DR CLYDE L CUMMER I should like to ask whether the appearance of the keratoses on the palms and soles at this relatively early stage is not unusual?

DR H A HAYNES JR. About five years ago a drug company developed a proprietary drug which was sold as a "blood tonic" and which contained a large amount of arsenic. Within eighteen months after patients began to take this preparation, they began to show the same type of pigmentation that this patient shows. I have observed about 12 cases relatively similar to this, with mottled small macular pigmentation, and in all of them keratoses had developed on the palms and soles within the eighteen months during which the patients had been taking this proprietary medicine. This may be an answer to the question as to how long it takes for these symptoms to develop.

Infectious Eczematoid Dermatitis Treated with Sulfanilamide. Presented by DR OTTO E L SCHMIDT

A C, a cement worker aged 52, presented from the department of dermatology and syphilology, Lakeside Hospital, had been suffering from an infectious eczematoid dermatitis of the hands, arms, face, buttocks and thighs since October 1938. He had been occasionally treated in the outpatient departments of the Lakeside Hospital and the City Hospital, with partial remissions followed by exacerbations. An exacerbation starting about one month prior to presentation had resisted the usual method of treatment.

On Oct 6, 1939, there were numerous infectious vesicular crusted lesions, with indolent ulcers, on the arms, buttocks and thighs. All local therapy was stopped, and sulfanilamide was given. He received 6 Gm. daily for two days and 4 Gm. daily for the subsequent seven days. At the end of forty-eight hours after this treatment was started, all lesions were undergoing involution. At the end of ten days only a few excoriated papules remained on the forearms.

A Case for Diagnosis (Capillaritis?). Presented by DR OTTO E L SCHMIDT

D L, a woman aged 38, presented from the department of dermatology and syphilology, Lakeside Hospital, has complained of swelling and tenderness over both shins for seven years. She had been hospitalized in 1932 for primary anemia and had responded poorly to liver and iron therapy. In 1935 she was again hospitalized, and diagnoses of primary anemia, grand mal epilepsy and edema and tenderness of the shins and ankles were made.

The patient was first observed in the outpatient department of dermatology at Lakeside Hospital on Feb 17, 1939. The condition on the legs has persisted for seven years. Various types of therapy, including roentgen irradiation, application

of zinc oxide glycerogelatin boots and rest in bed, have produced little or no improvement. There has been no ingestion of bromides or iodides.

The lesions at present are most noticeable on the anterior midportion of the right leg, consisting of an area of shiny, reddish brown, atrophic skin, 6 by 3 cm., with poorly defined, irregular edges. This area blanches incompletely on pressure, shows a moderate amount of edema and is tender on pressure. The surface presents numerous fine telangiectases. Two smaller lesions are present on the left shin.

The hemogram was normal. The basal metabolic rate on August 31 was —20 per cent. The patient was given thyroid.

Histologic examination showed that the epidermis was thin and had lost its interpapillary pegs. A slight degree of spongiosis was discernible here and there, particularly in places where there was some subepidermal edema. No hairs were found, but sweat glands with their excretory ducts were still present.

The principal change was in the corium, which was characterized by the presence of a large number of capillary blood vessels, particularly numerous in the subpapillary portion but also observed in the deeper parts of the corium. Their endothelial lining was thickened, often composed of two, or even three, layers of cells. The thickness made them look somewhat like sweat gland ducts. The nuclei projected occasionally into the lumen. The cytoplasm of the endothelial cells was more deeply stained with eosin than the neighboring connective tissue. As a result, these capillaries appeared encircled by a red ring. On sections stained for connective tissue, one occasionally recognized a second ring or circular connective tissue fibers outside the endothelial thickening. Deep in the corium large blood vessels with thickened walls and irregular lumens were seen.

In the corium there was a small amount of dark brown pigment, evidently hemosiderin, scattered throughout its whole thickness. The pigment granules were mostly between the connective tissue bundles. No pigment was observed in the cells. Red blood cells in small groups constituted tiny interstitial hemorrhages. Lymphocytes and polymorphonuclear leukocytes, few in number, were evenly, though sparsely, distributed in the corium.

A thick band of deeply stained fibrous connective tissue in coarse bundles, running parallel to the surface across the middle of the corium, was evidence of fibrosis.

It was concluded that the section represented a fairly good histologic picture of the advanced stage of "purpuric and pigmented angiodermatitis," as described by Favre.

DISCUSSION

DR OTTO E. L. SCHMIDT: The lesions have been present for the past seven years and have been resistant to all therapy so far. They have been resistant to diagnosis too. Perhaps Dr Miskjian could give us some ideas. He suggested capillaritis.

DR H. G. MISKJIAN: This syndrome has been described by Favre (Favre, M. *Angiodermite pigmentée et purpurique*, in Darier, J. *Nouvelle pratique dermatologique*, Paris, Masson & Cie, 1936, vol. 5, pp. 413-430). It seems to me that to any one who has read his description, the condition in this case is absolutely characteristic. The diagnosis is based on the fact that the large patch on the right leg is deep and dark red or purple. The lesion is evidently of vascular origin, and there are numerous pinhead-sized reddish spots, which are a manifestation of dilated capillaries. Another argument is that there are no varicose veins so far as we can ascertain. I know that the patient's leg swells a great deal if she is on her feet, she may have some deep varicose veins, but none are visible. Therefore, one cannot say that this condition is varicose dermatitis. In my estimation, varicose dermatitis is a somewhat outmoded loose term. The attempt of Favre to diagnose this condition as angiodermatitis or capillaritis when the primary cause is in the vascular system would explain why the condition is not always found associated with varicose veins.

DR HAROLD N COLE I was much interested in Dr Miskjian's discussion. The section shows a number of small newly formed vessels. From what part of the lesion was the section taken? On examination of the lesions on the patient's shins, the center shows some evidence of atrophy. I should like to suggest that another section be taken from the center.

DR H G MISKJIAN I should like to suggest that if a new biopsy is performed, the specimen should be taken rather deep, because Favre has described straight dilated capillaries which are gorged with blood and simulate multiple candles in a candle holder.

Lymphangioma and Multiple Hemangiomas in a Boy with Adiposogenital Dystrophy. Presented by DR HAL ELSON FREEMAN

R H, a man aged 19, presented from the department of dermatology and syphilology, Cleveland City Hospital, stated that he has had extensive red birth marks over his face, arms, trunk, right thigh and leg since birth. To his knowledge the right thigh and leg have always been larger and considerably longer than the left.

Since the age of 16 he has been observed and treated in the Department of Endocrinology of the City Hospital. It was noted that the external genitals were infantile. The testicles and prostate were much smaller than normal. The axillary and pubic hair was lacking, and his voice was high pitched. During this period he was treated by small doses of gonadotropic substances, including an extract of the anterior lobe of the pituitary gland (gynantrin) and a preparation from the urine of pregnant women (antophysin). Thyroid was also given. After this therapy his voice deepened, the genitals appeared normal and axillary and pubic hair appeared in normal amount.

On the right side of the face is a large port wine type of hemangioma. A similar type of nevus is on the back, on the right shoulder and on the right forearm. The entire right thigh, leg and foot is the seat of a diffuse nevus of the port wine type, resulting in a marked increase in size of the extremity. Comparative measurements show the circumference of the left knee to be 47 cm, while that of the right knee is 63 cm. The circumference of the left calf is 43 cm, and that of the right calf, 50 cm. The left leg is 4 cm longer than the right. His weight in September 1936 was 234 pounds (106 Kg), and in October 1939, 275 pounds (125 Kg).

Roentgenograms of the sella turcica and epiphyses were normal. The hemo-gram was normal.

DISCUSSION

DR CLYDE L CUMMER I should like Dr Freeman to explain the location of the lymphangioma.

DR HAL ELSON FREEMAN I considered the enlargement of the right thigh to be a lymphangioma.

DR GEORGE H CURTIS (by invitation) I agree with the diagnosis of adiposogenital dystrophy (Milroy's disease).

DR EMERSON GILLESPIE, Canton, Ohio Milroy's disease is familial and is practically always bilateral. It has a definite type of lesion. This man presents unilateral involvement, and I do not think that the condition could be classified as Milroy's disease.

DR J R DRIVER I believe that this process can be explained on the basis of hemangioma. He has port wine hemangiomas on the face, body, back and arms and also this enlargement of the entire right leg and thigh. The increased growth of bone is due to increased blood supply since infancy. While I would not want to say that there might not be some possibility of a mixture with a lymphangioma in the thigh, the fact that there is no evidence of that on the surface makes me believe that the whole process could be explained on the basis of hemangioma.

BRONX DERMATOLOGICAL SOCIETY

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Oct 26, 1939

Incipient Granuloma Inguinale Presented by DR. LOUIS CHARGIN

W. W., a Negro laborer aged 35, was admitted to the Central Social Hygiene Clinic of the Department of Health on Sept. 22, 1939, presenting a lesion on the shaft of the penis of nine weeks' duration.

On the dorsum of the lower third of the shaft is a well circumscribed ulceration the size of a dime. The base is a dirty gray, and the borders are raised and somewhat undermined. The lesion shows only slight induration. The inguinal lymph nodes are not enlarged. Dark field examination for spirochetes gave negative results. The Ito test (Lederle Ducrey bacillus vaccine) and the Frei test gave negative results. Smears for Ducrey bacilli were negative on repeated examination. In view of the fact that the lesion resembled chancreoid, sulfanilamide was administered for two weeks, without appreciable effect. At this time examination of smears revealed the presence of Donovan bodies.

DISCUSSION

DR. DAVID BLOOM: The fact that the lesion is somewhat raised and not deeply ulcerated, the absence of enlarged inguinal glands, the negative results of dark field examination and the long duration of the lesion force one to consider primarily granuloma inguinale. It has been my experience that it is rather difficult at times to demonstrate the Donovan bodies.

DR. DAVID L. SATENSTEIN: I do not doubt that the diagnosis is correct, but it must be stated that at this early stage a diagnosis of granuloma inguinale on purely clinical grounds is rather difficult. The diagnosis depends on the results of microscopic examination, i. e., on finding the organism. The ulceration is practically a primary lesion of the disease.

DR. DAVID BLOOM: The lesion is a typical one of the early stage of granuloma inguinale. Such lesions are likely to be seen more frequently at city hospitals. Early lesions are seen alone or in association with more advanced lesions of granuloma inguinale.

DR. CHARLES WOLF: In cases in which the organism cannot be demonstrated an efficient therapeutic test is to administer antimony and potassium tartrate (tartar emetic). An early lesion of this type should respond to two or three injections.

DR. SAMUEL M. PECK: As far back as 1924 I maintained in a publication with Dr. Leon Cornwall (*ARCH. DERMAT. & SYPH.* 12: 613-628 [Nov.] 1925) that the causative organism was a bacillus not of the Friedländer group. It has been forgotten that Goldzieher and I developed a cutaneous test analogous to the Frei test but specific for granuloma inguinale (*Vuchows Arch. f. path. Anat.* 259: 795-814, 1926). Also Kingsbury and I stated that antimony and potassium tartrate cannot be used for differential diagnosis as a therapeutic test in cases of granuloma inguinale, because antimony kills bacilli, protozoa and spirochetes (*J. A. M. A.* 87: 1900-1902 [Dec. 4] 1926). The organism apparently has not yet been definitely classified. As a matter of fact, many observers doubt that it has ever been cultured. It seems peculiar that one finds simultaneous lesions on the penis and in the inguinal region, with unaffected skin between. Yet the lymph nodes are not involved. The extension must be through the superficial lymphatics.

DR. LOUIS CHARGIN: I admit that on purely clinical grounds one could not make the diagnosis with any degree of certainty. It was the finding of the Donovan bodies that established the diagnosis. The clinical diagnosis was really arrived at largely by exclusion, since chancreoid, chancre and lymphogranuloma

venereum could be ruled out. The disease is not apparently as rare as it appears. Greenblatt, Dienst, Pund and Torpin recently reported a number of cases of granuloma inguinale (*J A M A* 113:1109 [Sept 16] 1939), they discussed this type of lesion and also attempted to explain that while the disease does not attack the lymph glands, it attacks the overlying tissues, producing a pseudobubo. They also called attention to the fact that antimony and potassium tartrate is by no means a specific remedy for any disease. Therefore, it cannot be used to diagnose this disease. Weidman is of the opinion that the organism is probably a fungus.

Acne Urticata Polycythaemica Presented by Dr ADOLPH ROSTENBERG

A man, a real estate operator aged 52, gives an irrelevant family history. He had the usual diseases of childhood. He was operated on for an inguinal hernia about twenty years ago. The present illness began about one and one-half years ago, with dizziness, frequent headaches and general malaise. The patient noticed that the skin assumed a dusky appearance and that the eyes became blood shot. He occasionally had bloody stools but no bleeding from the nose or mouth. He suffered from a moderate cough, with mucoid expectorations, and lost about 15 pounds (68 Kg) during the last two years. About eighteen years ago he had gonorrhea without complications. He states he had no other venereal infections. The eruption began with severe itching in the pelvic region and soon spread to other parts of the body. The lesions appeared in crops.

The entire skin is livid. In the lumbar region a diffuse squamous eczematous eruption predominates. On the trunk and extremities there are numerous dark reddish papular lesions, ranging in size from that of a lentil to that of a large pea. Some of the lesions show definite wheals, while others are topped by an adherent crust or by small pustules. On the extremities there are lesions that have undergone involution, leaving superficial scars and pigmentation. Many lesions on the trunk are scratched and strongly resemble neurotic excoriations. The physical examination revealed a moderately well nourished man with flabby muscles. The conjunctivas and all the mucous membranes were congested. The heart was slightly enlarged. The apex beat was displaced to the left. No murmurs were present. The pulse rate was 108 per minute. The systolic blood pressure was 125 and the diastolic 90. The lungs showed evidence of chronic bronchitis. The liver and spleen were enlarged. The inguinal glands were visible, hard and indolent, some were of walnut size.

Examination of the blood showed 145 per cent hemoglobin (Sahli method), a color index of 0.88, and 8,230,000 red cells and 6,150 white cells per cubic millimeter, with 59 per cent segmented forms, 23 per cent lymphocytes, 5 per cent band forms, 3 per cent eosinophils, 4 per cent basophils and 6 per cent monocytes. Poikilocytosis, anisocytosis and hyperchromia were present. The sedimentation rate (Westergren method) was strongly delayed, it was 0.25, 0.5 and 5.5 mm in one, two and twenty-four hours, respectively. The Wassermann reaction was negative. Examination of the urine showed a trace of albumin but no sugar or acetone. Urobilinogen was present. On sedimentation there were many erythrocytes, granular and hyaline casts and a few leukocytes. Fluoroscopic examination showed an aortic configuration of the heart, with hypertrophy of the left ventricle. There was evidence of chronic bronchitis.

Histologic examination showed that the vessels of the subepidermal zone were dilated and empty, almost telangiectatic. The vessels of the deep portion of the cutis were dilated and filled with blood cells but were not thrombosed. The walls of the superficial vessels were somewhat swollen, in the deeper part of the cutis there was a varying degree of proliferating endarteritis. There was a sparse, predominately perivascular cellular infiltrate. This was composed of a few polymorphonuclear leukocytes, some small round cells (monocytes), a few scattered mast cells and a considerable number of histiocytes (reticulum cells). The epidermis was similar to that noted in patients with neurodermatitis. The histologic findings suggested a reticuloendothelial reaction.

Acetylphenylhydrazine was given in courses of seven days with intervals of five days. Roentgen ray treatments in fractional doses were given to the affected parts at weekly intervals. The response to this treatment was favorable, with regard to cutaneous lesions and blood picture. The erythrocyte count diminished from 8,230,000 to 4,970,000 per cubic millimeter, and the hemoglobin, from 145 to 120 per cent. The subjective symptoms disappeared, and the eruption showed considerable improvement. The patient has gained 8 pounds (3.6 Kg), and the entire condition is at present in a regressive stage.

DISCUSSION

DR ISIDORE M LASHINSKY. The relation between polycythaemia vera and this cutaneous disease is somewhat difficult to understand. In view of the more frequent occurrence of polycythaemia vera it is rather rare to find the combination. Dr Rostenberg's authentic case together with the 8 cases of acne urticata polycythaemica recorded by Weidman and Klauder give a total of 9 cases in a period of seventeen years.

DR LOUIS CHARGIN. In former days this type of eruption was diagnosed as leukemid. The lesions were papular and pruriginous and were associated with one of the blood diseases, usually leukemia. Conditions of this type were also called neurotic excoriations of the skin. On clinical grounds I do not know how to make this particular diagnosis without the benzidine test. Acne urticata is not an integral part of polycythemia.

DR CHARLES WOLF. In a long experience with many patients with polycythaemia vera that came under my treatment in the roentgen department of Mount Sinai Hospital I have seen urticarial papular lesions associated with this disease in but 2 cases. The lesions I refer to were reddish, mildly itchy papules, which occurred around the nose, on the chest and on the back. They never broke down to produce ulceration, such as seen in this patient. Clinically the lesions in this patient suggest prurigo nodularis. In view of this resemblance it is questionable whether the condition is acne urticata polycythaemica.

DR ADOLPH ROSTENBERG. The case presented is practically a counterpart of that reported by F D Weidman and J V Klauder (*ARCH DERMAT & SYPH* 39 645 [April] 1939) under the title "Acne Urticata Polycythaemica". The principal feature of this disease is an extensive papular eruption which, being pruriginous, is often scratched, and then the lesions resemble neurotic excoriations. According to Weidman the diagnosis of this entity depends on the finding of staining for oxidase in the cells of the papular lesions. Unfortunately I have been as yet unable to perform this test.

Pemphigus Erythematodes (Senear-Usher). Presented by DR HENRY SILVER

The patient, a woman aged 41, was presented at the meeting of this society on Nov 22, 1934 (*ARCH DERMAT & SYPH* 31 923 [June] 1935).

From November 1934 to September 1937 she was treated with intermittent courses of bismuth subsalicylate. On Sept 11, 1937, after prolonged exposure to the sun, new lesions appeared on the upper part of the arms. They were arranged in a semicircle and had a tendency to spread upward. The lesions apparently began as bullae but soon ruptured, forming thick crusts. The eruption cleared, leaving slight pigmentation.

On Aug 5, 1939, this time without exposure to the sun, bullous lesions appeared on the right ear, in the midsternal region and on the upper part of the arms. The areas showed the same characteristic thick crust and rapid healing without a trace of atrophy. There are still a number of active lesions of typical lupus erythematosus on the nose and scalp and behind the ears.

Histologic examination of a lesion taken from the arm showed that a greater part of the lesion was taken up by a thick crust which embraced a good deal of necrotized epidermis. The tissue under it showed considerable inflammatory reaction.

DISCUSSION

DR. LOUIS CHARGIN. An attempt should be made to clarify the subject of the Senear-Usher syndrome. Although I do not think that the problem will be settled here tonight, the discussion may help to bring about a clearer understanding of this subject, on which there is much confusion. It is my impression that Senear and Usher originally presented their material with the idea of describing a variety of pemphigus in which no bullae are seen or in which bullae rupture rapidly and produce superficial scaly crusts. The eruption bears a resemblance to seborrheic eczema. True lupus erythematosus with bullae was also included in that syndrome. It seems to me that one should either drop the term or agree to call one condition or the other Senear-Usher syndrome and not apply the name to two diseases that are unlike in their course and from every other standpoint.

To make my view clearer, may I state that when a patient has syphilis with psoriasiform lesions one does not call the condition psoriasis, it is syphilis with a psoriasiform type of lesion. Conversely, when a patient presents psoriasis which resembles syphilis, the condition is psoriasis and not syphilis. The two diseases are distinct and should not be confused with each other. I think that the Senear-Usher syndrome should be limited to one disease, and I have the impression that the authors meant to apply it to a type of pemphigus. One can say that a given condition is a Senear-Usher type of pemphigus or, if one wishes to broaden the concept, that it is a Senear-Usher type of lupus erythematosus, but one cannot bring two distinct diseases under this heading, otherwise there will always be confusion.

DR. MAURICE UMANSKY. In the majority of the cases reported under the caption of Senear-Usher syndrome there were elements of disseminated lupus erythematosus. The woman presented tonight had undoubtedly lesions of the discoid variety of lupus erythematosus. In the original collection of cases described by Senear and Usher there was 1 case in which the last-mentioned form of lesions were present. The presenter was therefore justified in bringing up the question of classifying his case in the group of cases known under the name of Senear-Usher syndrome.

DR. HENRY SILVER. When I first presented this patient in 1934 I called particular attention to the lesions on the arms and chest, which were at variance with the typical lesions of lupus erythematosus on the face and scalp. At that time I pointed out that such conditions were recorded as belonging to the Senear-Usher syndrome. What Senear and Usher originally described was an unusual type of pemphigus combined with clinical features of lupus erythematosus. Later on the entire concept was confused, and lupus erythematosus with bullous and crusted lesions was also regarded as characteristic of the syndrome. It has always seemed to me somewhat artificial to combine two totally unrelated diseases, the causes of which are still unknown, in a new syndrome. I think that one can safely dispense with the concept of the Senear-Usher syndrome.

Poikiloderma of Civatte. Presented by DR. HARRY B. FEILER

M. A., a woman aged 33, born in the South, was admitted to the clinic of the Lebanon Hospital about three months ago. Since January 1939 she has had a persistent eruption on the face unaccompanied by itching or scaling. The eruption is stationary and at times is more conspicuous. It involves both eyelids and extends over the adjacent parts of both zygomas and the nasolabial folds downward along the sides of the chin and the lateral part of the neck. It presents a mottled appearance, consisting of reddish lesions, telangiectasis and brownish pigmentation. There is no sign of atrophy. The Wassermann reaction was negative.

Histologic examination of a section taken from the left side of the neck showed a disorganization and vacuolation of cells of the basal layer of the epidermis. Fine granules of pigment were scattered in this area. The subepidermal vessels were dilated, and the walls were edematous. The cutis framework surround-

ing the vessels was finely reticulated, in the upper part of the cutis there was considerable vacuolation. There was some suggestion of a mild degree of basophilic degeneration of the collagen. The elastic tissue was in part wanting in the areas of edema. There was a sparse small round cell infiltrate in the perivascular lymph spaces. These findings corroborated the clinical diagnosis as presented and suggested an early stage of the disease.

DISCUSSION

DR DAVID L. SATENSTEIN: From the histologic standpoint the features present are not typical of poikiloderma of Civatte, so that one cannot make a positive diagnosis. However, the telangiectasia seems to suggest an early stage of the disease.

DR ARTHUR SAYER: The essential clinical features of Civatte's poikiloderma are found in this patient. The eruption is usually seen in women and is limited to the face and neck.

DR CHARLES A. GREENHOUSE: In spite of the limitation and location of the eruption on the face only, I feel that this case is clinically one of poikiloderma of Jacobi, because the entire picture appears to simulate closely a roentgen ray dermatitis.

DR MARION B. SULZBERGER: It appears to me that clinically this condition is poikiloderma. There is telangiectasia, mottling and pigmentation (although the latter is not pronounced), which in combination are characteristic of poikiloderma. Any one at first glance would think that the condition was probably a sequela of roentgen irradiation. The sex and age of the patient and the localization of the eruption indicate that the condition is Civatte's poikiloderma. Many identify Civatte's poikiloderma with Riehl's melanosis or Hoffman's melanodermatitis toxica. However, I believe that this entity has no resemblance to the active stage of Riehl's melanosis. There is much more pigmentation, papulation and inflammation in early Riehl's melanosis than in Civatte's poikiloderma. The end stages of both diseases may be indistinguishable. I do not think that one can call the condition in this case Jacobi's poikiloderma, since there are no lesions on the favorite sites, i. e., on the trunk. Moreover, for obvious reasons, the Petges-Clejat type and the Jaffe-Rotman type can be excluded.

DR DAVID L. SATENSTEIN: I have treated such conditions with the vacuum cup method. The suction ruptures the blood vessels. If this treatment is used for an extended period, the lesions gradually disappear.

Epidermolysis Bullosa Acquisita Presented by DR LEO SPIEGEL

P. E., a fireman aged 57, first came to the clinic of the Lenox Hill Hospital in 1926, for treatment of syphilis. The Wassermann reaction was 4 plus with both alcoholic and cholesterolized antigens. He has been under treatment and observation since that time. Since 1933 serologic tests and examination of the spinal fluid have given negative results. Cardiac examination showed tremendous enlargement of the cardiac and aortic shadows, compatible with advanced hypertension. There was probably an aneurysmal dilatation with aortic regurgitation. The wall of the aorta was heavily calcified.

About four months ago the patient began to complain that whenever he injured the fingers or hands, painful blisters and sores appeared on the injured parts. Since then vesicles and blisters have continued to appear, so that now many lesions are present on the forearm. There are numerous erosions, areas of pigmentations and scars from previous lesions distributed over the parts mentioned. The vesicles and bullae are distended with clear fluid and appear to arise from apparently normal skin; there is no erythema at the base of the lesions. Nikolsky's sign could not be elicited. There has been no loss of weight. The patient states that he has not ingested any drugs.

The urinalysis gave negative results on several occasions. The blood count showed 5,600,000 red cells and 8,450 white cells per cubic millimeter, with 35 per

cent polymorphonuclear leukocytes, 61 per cent lymphocytes, 2 per cent large mononuclears, 1 per cent eosinophils and 1 per cent basophils. The phytopharmacologic test gave a reading of 59 per cent. The sedimentation rate (modified Westergreen method) was 11 mm in fifteen minutes.

Tertiary Syphilis and Syphilitic Macular Atrophy. Presented by DR ADOLPH ROSTENBERG

A Negress aged 28 was first admitted to the Bronx Hospital on May 31, 1939, with a diagnosis of actinomycosis of the left jaw, made by her physician and based on a laboratory report. The patient stated that five weeks previously a tense, hard and painful swelling had appeared at the angle of the left jaw. One week later she had noticed another swelling in the left submaxillary region. There had been no infection of the upper part of the respiratory system accompanying these lesions.

The patient had lived in the South prior to admission to the hospital. She had been in good health until ten years ago, at which time the left submaxillary gland became swollen, it was incised and pus was expressed. About that time she was told that her "blood was bad" and was given six injections in the "arm." Four years later severe parietal headaches developed, which lasted continuously for two weeks. No diagnosis was made at that time, and the patient was well after two weeks. A year later she had "stomach trouble," and a diagnosis of "ulcers" was made. There was no roentgenographic confirmation of the diagnosis. Since then the patient has suffered from intermittent abdominal pain. The cutaneous lesions have been present for many years.

There is a soft red fluctuating mass about the size of a plum situated anteriorly at the angle of the left jaw. The submaxillary gland on the same side is enlarged and slightly tender. The deep reflexes are sluggish. There are three distinct types of lesions: (1) atrophic, partially depigmented wrinkled soft macules the size of a pea scattered over the back and chest, with a few over the thighs and the lower parts of the legs, (2) keloid-like pigmented lesions (about a dozen scattered over the trunk, extremities and buttocks) and (3) minute pale atrophic macules not larger than a pinhead.

Examination of the blood showed 6,000 white cells, with 67 per cent lymphocytes, 32 per cent polymorphonuclear leukocytes and 1 per cent monocytes. Examination of the urine gave negative results. Chemical examination of the blood gave negative results. Roentgenograms of the jaw and lungs revealed no abnormalities. The Wassermann reaction was 4 plus.

The abscess was incised. Cultures were sterile, and no ray fungi were seen. A paraffin section of the fixed material did not show evidence of actinomycosis. Because of the conflicting laboratory reports concerning the presence of actinomycosis more detailed studies were undertaken. The lesion of the jaw was aspirated. Smears showed a few gram-positive cocci. A search for tubercle bacilli, Donovan bodies and actinomycetes gave negative results. Of culture *Staphylococcus aureus* grew. The result of a tuberculin test was strongly positive.

Reexamination of the patient for tuberculosis, including roentgenograms of the jaw and chest, gave negative results. The Frei test gave negative results. The Wassermann reaction was 4 plus on repeated examination.

Sections were taken from various cutaneous lesions. The large pale atrophic lesion showed on microscopic examination considerable hyaline change involving the connective tissue of the cutis and the subcutis. Elastic tissue was absent. The keloid-like lesions showed a moderate amount of hyperkeratosis with pigmentation of the basal layer of the epidermis. The underlying connective tissue was hyalinized. Another section showed embedded in the subcutaneous tissue a well demarcated bluish-staining mass, consisting of rather cellular connective tissue. Many of the cells were large and contained pyknotic nuclei.

The patient is receiving antisyphilitic therapy. The lesion showed regression after four weeks. The skin has remained unchanged except for the development of moderate keloids where biopsy specimens were taken.

DISCUSSION

DR DAVID L SATENSTEIN I think that the presenter needs more proof when he contends that the condition is macular atrophy following a syphilitic eruption. It is my impression that the condition is macular atrophy in a syphilitic patient, not the type that follows a syphiloderm.

DR ADOLPH ROSTENBERG I must admit that it is difficult to differentiate a syphilitic from a nonsyphilitic macular atrophy. The patient has been suffering from syphilis for many years, and it therefore seems reasonable to assume that the macular atrophy is syphilitic.

DR HENRY SILVER Can Dr Satenstein differentiate histologically syphilitic macular atrophy from macular atrophy occurring in a syphilitic patient?

DR DAVID L SATENSTEIN Atrophy subsequent to involution of a syphilitic lesion shows histologic evidence of syphilis. Clinically the atrophic lesions will be of the same size as the syphilitic lesions they replace, but not so elongated. Macular atrophy does not occur, as far as I know, in association with secondary syphilitic lesions; it occurs with tertiary lesions. On the other hand, macular atrophic lesions not on a syphilitic basis show the usual pathologic changes of macular atrophy, i. e. a loss of elastic tissue and no evidence of a syphilitic process.

DR DAVID BLOOM I wish to suggest that the left cervical adenitis is not due to syphilis but to tuberculosis. The patient has received adequate antisyphilitic therapy to have caused complete involution of the lymph gland tumor if it were due to syphilis. The strong tuberculin reaction speaks also in favor of tuberculous adenitis. A roentgenogram of the chest and graded tuberculin tests are indicated.

DR LOUIS CHARGIN In this particular case it is difficult to trace the relation between the macular atrophy and syphilitic infection, since there is no definite evidence that such transition took place. The presenter must be able to rule out tuberculosis before accepting the condition as syphilis.

DR SAMUEL FELDMAN Macular atrophy in a syphilitic patient recently under my observation followed a lichenoid follicular syphilid (*ARCH DERMAT & SYPH* 38 504 [Sept] 1938). The lesions were extremely minute, and because of this some of the discussers were doubtful that the condition was macular atrophy. There was herniation, although the lesions were too small for the herniation to be felt by the palpating finger.

DR HENRY SILVER While I agree with Dr Chargin's statement, I think that the point should be emphasized that one cannot definitely state that macular atrophy actually followed a syphilitic eruption. This process, as a rule, cannot be evaluated clinically, and that is why I asked Dr Satenstein whether it is possible to differentiate histologically. Unless there is clinical evidence of transition or at least a history indicating that the associated macular atrophic lesions followed preexisting syphilitic lesions, one cannot diagnose syphilitic macular atrophy. Otherwise one has to assume that the macular atrophy coexists in a syphilitic patient.

Recurrent Bullous Eruption (Duhring's Disease?) Treated with Trichophytin Presented by DR SAMUEL M PECK and DR HERBERT ROSENFELD (by invitation)

B. H., a man aged 63, was first seen at Mount Sinai Hospital in 1936, because of asthma and hay fever of thirteen years' duration. In March 1939 he was seen because of an eruption which had been present for five months. The skin at that time showed groups of large bullous lesions on an erythematous base on the soles, ankles, wrists and arms. The mucous membranes were free of lesions. Itching was a prominent symptom. The lesions healed, leaving pigmented areas. Between the toes there was typical dermatophytosis.

Examination of the blood showed 96 per cent hemoglobin and 10,000 white cells per cubic millimeter, with 51 per cent segmented polymorphonuclear leukocytes, 9 per cent nonsegmented cells, 27 per cent lymphocytes, 3 per cent monocytes and 10 per cent eosinophils. Chemical examination of the blood showed 15 mg of urea and 130 mg of sugar per hundred cubic centimeters, and 160 mg of cholesterol ester and 260 mg of cholesterol per hundred cubic centimeters. Cultures from cutaneous lesions revealed *Staphylococcus aureus*. The basal metabolic rate was -3 per cent. The urine showed a faint trace of albumin. A roentgenogram of the chest was normal.

The patient was hospitalized and received roentgen ray treatment, sulfapyridine, arsenic by injection and by mouth and mapharsen by continuous intravenous drip, consisting of three doses of 0.1 Gm each. He improved slightly under this regimen. On July 11, after he was discharged from the hospital, the eruption became aggravated. Sulfanilamide was administered, but no improvement was seen. Potassium iodide given for his asthma caused exacerbation. The trichophytin test caused a local bullous reaction. The lesions, however, were microscopically and culturally negative for fungi. Since that time he has received fifteen injections of trichophytin, with substantial improvement. He is presented tonight practically free of lesions for the first time in months.

DISCUSSION

DR CHARLES WOLF Various diagnoses were suggested in this case, among which were pemphigus, bullous erythema, bullous trichophytid and drug eruption. Dr Peck suggested Duhring's disease. The question still remains open whether the patient has a fungous infection which could not be established by culture but responded to specific therapy or another disease which has responded to non-specific therapy.

DR MARION B. SULZBERGER I think that the condition in this case is undoubtedly Duhring's disease, and the improvement may or may not have any connection with the injections of trichophytin. Assuming that the improvement is in any way attributable to the trichophytin, the therapeutic effect may have been either specific or nonspecific.

DR SAMUEL M. PECK The patient had been subjected to all sorts of therapeutic procedures prior to the use of trichophytin. Since there was a decided sensitivity to potassium iodide, Duhring's disease was considered. It is well known, however, that other bullous eruptions occasionally give a so-called flare-up after injections of potassium iodide. Since there was a local bullous reaction after injections of trichophytin, the possibility that the eruption was a dermatophytid had to be considered, especially since the patient presents dermatophytosis between the toes. It was for this reason that he was given injections of trichophytin. He seemed to improve rapidly under this form of therapy.

Generalized Lichen Planus with Lesions of the Palms and Nails Presented by DR ARTHUR SAYER

A R., a widower aged 76, born in Russia, a retired tailor, came to the clinic of Mount Sinai Hospital on Dec 20, 1934, presenting an extensive itching eruption of a few weeks' duration. The eruption was typical of lichen planus, with many flat-topped shiny polygonal and umbilicated lesions scattered over the trunk and extremities. On the palms were numerous discrete papules, which clinically did not resemble the lesions on the other parts of the body. The palmar papules were itchy and seemed to merge on the wrists with groups of typical lesions.

The patient received injections of sodium arsenate from December 25 to March 9, 1935. He was given superficial roentgen therapy to relieve the itching. On August 29 he still had an extensive eruption on the body, including the palmar lesions. He was then referred to the department of roentgenology for deep para-

vertebral irradiation He received 250 r to each field from the cervical to the lumbar region, with a filter of 0.5 mm of copper and 1 mm of aluminum

On Feb 16, 1936, the palms were entirely free of lesions, and the eruption on the body was rapidly undergoing involution On May 16 the skin was normal in all respects He remained well for about three and one-half years On Aug 31, 1939, he returned to the clinic presenting a fairly generalized eruption

On the thighs, abdomen and upper extremities the lesions are flat topped, shiny and violaceous On the dorsa of the hands there are hypertrophic violaceous lesions A whitish reticulated patch is present on the right buccal mucosa On the palms are many papules which do not resemble clinically the papules of lichen planus on the body but merge with shiny flat-topped violaceous papules There are tiny violaceous lesions which can be seen through the nail plate, they are arranged in parallel longitudinal lines

Histologic examination of a lesion from the right palm showed hyperkeratosis with a few scattered vesicles in the keratin layer There were also areas of parakeratosis The epidermis, while acanthotic in places, showed flattening of the papillary bodies by an infiltrate lying directly beneath it and consisting mainly of lymphocytes The line between the cutis and the epidermis was indistinct and showed edema and invasion of leukocytes The picture strongly suggested lichen planus

On October 29 the lesions on the palms were retrogressing During the past six weeks the patient has received injections of bismuth subsalicylate and solution of potassium arsenite (Fowler's solution) by mouth

DISCUSSION

DR. FRANK E. CROSS The extensive recurrence of the lichen planus does not appear to justify the enthusiasm for the paravertebral method of therapy

DR. ARTHUR SAYER The reason for presenting this patient is to show the unusual palmar lesions and the lesions in the nail bed which I believe to be true lichen planus of the nails The palmar lesions closely resemble the picture described by Fordyce and MacKee in their article on clinical types of lichen planus (*J Cutan Dis* 37 320, 1919) They specifically stated that lichen planus of the palms does not look like ordinary lichen planus, but the lesions are large, deep seated and semitranslucent and suggest deep-seated vesicles After injections of bismuth subsalicylate the palmar lesions have retrogressed considerably, and the lesions on the body are fading, but the lesions of the nails have remained stationary

Syphilitic Leukoderma Following a Secondary Papular Eruption. Presented by DR. LOUIS CHARGIN

J. J., an unmarried Negro factory worker aged 23, born in the United States, had a penile sore during March 1937 Soon thereafter there developed a generalized eruption consisting of "pimples" the size of the present white lesions He had no treatment at the outset, but some weeks later he received 5 "arm" and 15 "hip" injections, after which the eruption disappeared, leaving the present leukodermic areas These have not changed, in spite of continued intravenous therapy

The lesions, which are leukodermic spots, are located over the entire back, abdomen and legs There are a few scattered lesions on the arms The lesions are round, white, the size of a large pea and for the most part isolated There is, however, in a few areas group and segment formation A number of lesions show in the white areas a small central pigmentation resembling leukoderma acquisitum centrifugum The borders of the lesions are not hyperpigmented, as in vitiliginous lesions The skin of the affected areas is entirely smooth and is neither raised nor depressed

The Wassermann reaction was 4 plus

DISCUSSION

DR WILBERT SACHS Were any of the secondary lesions annular?

DR DAVID BLOOM Did the preceding syphilitic eruption consist of papules or pustules?

DR LOUIS CHARGIN As far as it was possible to ascertain, there were no annular or pustular lesions present. I am accepting the patient's definite statement that the white spots appeared at the site of the generalized eruption. This type of leukoderma is not common. It differs from leukoderma colli, which, in my opinion, is rarely preceded by a macular or papular eruption. I recall a similar case about fifteen years ago which I was able to follow from the beginning of the papular eruption to the appearance of the leukoderma. I have never seen this kind of lesion before, and it is of interest.

**Dermatitis Eczematosa (Contact Type) Due to Nickel. Presented by
DR MARION B SULZBERGER**

Miss R. L., aged 24, noticed in July 1939 a rash behind the ears. Since then other areas have become involved: the left cubital space, the left wrist and the back. In all these areas the patient has been in contact with articles presumably containing nickel (rims of spectacles, metal part on handbag, wrist watch and metal piece on brassiere). The patient presents erythematous squamous ill defined areas in the sites mentioned. Patch tests with a 5 per cent solution of nickel sulfate gave a 4 plus reaction, and with scrapings from the metal rims of the eyeglasses, a 2 plus reaction.

DISCUSSION

DR ARTHUR SAYER What value does Dr Sulzberger place on the results of patch tests performed with nickel? Nickel is rather notorious for giving positive reactions in nearly all persons. For that reason I believe that a positive reaction to a patch test does not signify a true sensitivity to this metal.

DR FRANK E. CROSS A woman under my observation displayed a hypersensitivity to the nose-piece of the eyeglasses, fasteners on the brassiere, the wrist watch, metal on the garters and earring at the same time.

DR MARION B. SULZBERGER I want to call attention to a site of typical localization which has been insufficiently stressed in cases of nickel dermatitis. In women with nickel sensitivity one often finds lesions not only in areas in contact with spectacles, the metal part of garters, clasps, hooks, eyes and zippers but also in the bend of the arm, due to the carrying of handbags. This site is due to exposure to the metal clasps and other decorative metals of handbags, which are often carried in such fashion that the metal touches the cubital space and the adjacent areas of the arm and forearm. Patch tests with nickel do not give positive results in everybody if used in the right concentration. Two to 5 per cent nickel sulfate causes no reactions in normal skins. This nickel salt will not cause a positive eczematous response unless there is a real eczematous sensitivity to nickel. However, in atopic dermatitis nickel tests not infrequently give positive results, but this reaction is not eczematous. The reaction does not look the same as in contact type dermatitis, either clinically or histologically.

**Discoid Lupus Erythematosus Improved with Germanin. Presented by
DR SAMUEL M. PECK**

B. B., a woman aged 27, was presented before this society in May 1939 (ARCH DERMAT & SYPH 40:858 [Nov] 1939). She is presented now to demonstrate the result of treatment with germanin, which was concluded at the end of the summer. She has received in all fifteen injections of germanin, given once weekly. With the exception of one spot the size of a dime, which still has the characteristics of lupus erythematosus, the previous extensive eruption of the face has disappeared without leaving a trace. During the summer the patient was told to expose herself to sunlight, at beaches, for instance, which she did. There was no flare-up of old lesions, and no new lesions have developed.

DISCUSSION

DR ARTHUR SAYER I would hesitate to give germanin to ambulatory patients because of the risk of a sudden serious reaction

DR LOUIS CHARGIN The results obtained in this case of lupus erythematosus are indeed good. However, one must be cautious with germanin, and one must not draw conclusions from the results in 1 case

DR MARION B SULZBERGER I do not think that it is correct to say that germanin is "a dangerous drug." Gold is surely just as dangerous, and yet most of us give a gold compound routinely in the treatment of lupus erythematosus, a condition much less serious than pemphigus. I think that it is unfortunate that in all probability germanin cannot be tried much longer in this country, as I believe it to be a useful addition to the therapeutic drugs for several dermatoses, including pemphigus, dermatitis herpetiformis and lupus erythematosus. I have for several years tried in vain to obtain the French preparation of germanin, which is manufactured by the Pasteur Laboratories. For some reason the French drug is at present unobtainable in America.

DR SAMUEL M PECK I had hoped to present 2 cases tonight, both of which have been previously shown before the society (*ARCH DERMAT & SYPH* 40 858 [Nov] 1939). In this way one could judge the results of treatment and follow the progressive improvement. The patient who failed to appear was a man with persistent lesions on the face, as you may recall. The first report on the use of germanin in lupus erythematosus appeared about a year ago (Chajes, B *Lancet* 2 1288 [Dec 3] 1938). The reason for its use in the 2 cases I presented was the resistance of the condition to all previous forms of therapy, including gold compounds, bismuth compounds and sulfanilamide. A rather unusual result of germanin therapy is the apparent desensitization to light. If this effect is true, germanin should be the drug of choice for this condition.

News and Comment

EXAMINATION FOR CERTIFICATION BY THE AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

The American Board of Dermatology and Syphilology has decided to hold an examination for certification by the Board in New York on June 10 and 11, 1940, at the time of the meeting of the American Medical Association. The written examination will be held in various cities of the country on Monday, April 29, 1940. Applications for group A candidates will be accepted until May 1, 1940.

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